

GenCore version 5.1.6
Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:38:32 ; Search time 49.3333 Seconds
(without alignments)
3991.938 Million cell updates/sec

Title: US-09-806-194A-18
Perfect score: 3651
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 1586107 seqs, 282547505 residues

Total number of hits satisfying chosen parameters: 1586107

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_29Jan04:*
1: geneseqp1980s:*
2: geneseqp1990s:*
3: geneseqp2000s:*
4: geneseqp2001s:*
5: geneseqp2002s:*
6: geneseqp2003as:*
7: geneseqp2003bs:*
8: geneseqp2004s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	%		DB	ID	Description
		Query	Match Length			
1	3651	100.0	697	3	AAy88429	Aay88429 Human APP
2	3651	100.0	697	4	AAU07209	Aau07209 Human bet
3	3651	100.0	697	4	AAE10636	Aae10636 Human amy
4	3651	100.0	697	4	AAE06866	Aae06866 Human amy
5	3651	100.0	697	4	AAE02588	Aae02588 Human amy
6	3651	100.0	697	4	AAU06610	Aau06610 Human Amy
7	3651	100.0	697	5	ABB78597	Abb78597 Human APP
8	3643	99.8	697	3	AAy88428	Aay88428 Human APP
9	3643	99.8	697	4	AAU07208	Aau07208 Human bet

10	3643	99.8	697	4	AAE10635	Aae10635	Human	amy
11	3643	99.8	697	4	AAE06865	Aae06865	Human	amy
12	3643	99.8	697	4	AAE02587	Aae02587	Human	amy
13	3643	99.8	697	4	AAU06609	Aau06609	Human	Amy
14	3643	99.8	697	5	ABB78596	Abb78596	Human	APP
15	3641	99.7	695	3	AAAY88435	Aay88435	Human	APP
16	3641	99.7	695	4	AAU07206	Aau07206	Human	bet
17	3641	99.7	695	4	AAE10633	Aae10633	Human	amy
18	3641	99.7	695	4	AAE06863	Aae06863	Human	amy
19	3641	99.7	695	4	AAE02585	Aae02585	Human	amy
20	3641	99.7	695	4	AAU06607	Aau06607	Human	Amy
21	3641	99.7	695	5	ABB78594	Abb78594	Human	APP
22	3641	99.7	695	7	ADB87313	Adb87313	Human	amy
23	3638	99.6	697	3	AAAY88430	Aay88430	Human	APP
24	3638	99.6	697	4	AAU07210	Aau07210	Human	bet
25	3638	99.6	697	4	AAE10637	Aae10637	Human	amy
26	3638	99.6	697	4	AAE06867	Aae06867	Human	amy
27	3638	99.6	697	4	AAE02589	Aae02589	Human	amy
28	3638	99.6	697	4	AAU06611	Aau06611	Human	Amy
29	3638	99.6	697	5	ABB78598	Abb78598	Human	APP
30	3638	99.6	740	7	ADB87314	Adb87314	Human	amy
31	3638	99.6	740	7	ADB87312	Adb87312	Human	amy
32	3636	99.6	695	2	AAW19490	Aaw19490	APP695	mu
33	3636	99.6	695	2	AAW19504	Aaw19504	APP695	mu
34	3633	99.5	695	1	AAP81692	Aap81692	Sequence	
35	3633	99.5	695	2	AAR26338	Aar26338	APP695.	3
36	3633	99.5	695	2	AAAY20233	Aay20233	Human	bet
37	3633	99.5	695	2	AAAY07221	Aay07221	Amyloid	p
38	3633	99.5	695	3	AAAY88434	Aay88434	Human	APP
39	3633	99.5	695	3	AAAY44705	Aay44705	Human	bet
40	3633	99.5	695	4	AAE10632	Aae10632	Human	wil
41	3633	99.5	695	4	AAE06862	Aae06862	Human	wil
42	3633	99.5	695	4	AAE02584	Aae02584	Human	amy
43	3633	99.5	695	4	AAU06606	Aau06606	Human	Amy
44	3633	99.5	695	5	ABB78593	Abb78593	Human	APP
45	3633	99.5	695	5	AAG68315	Aag68315	Human	amy

ALIGNMENTS

RESULT 1

AAAY88429

ID AAY88429 standard; protein; 697 AA.

XX

AC AAY88429;

XX

DT 03-AUG-2000 (first entry)

XX

DE Human APPSW-KK amino acid sequence.

XX

KW Aspartyl protease; aspartase; amyloid precursor protein; APP; Asp 2;

KW Alzheimer's disease; beta secretase site; APPSW-KK.

XX

OS Homo sapiens.

XX

PN WO200017369-A2.

Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDGDEVEEEAEEPVEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDGDEVEEEAEEPVEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEI SEVNLD AEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEI SEVNLD AEF	600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITL VMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITL VMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697

RESULT 2

AAU07209

ID AAU07209 standard; protein; 697 AA.

XX

AC AAU07209;

XX

DT 24-OCT-2001 (first entry)

XX

DE Human beta-amyloid protein precursor, APP695-Sw-KK.

XX

KW Human; aspartyl protease 1; Asp-1; nootropic; neuroprotective;

KW aspartyl protease 2; Asp2; amyloid protein precursor; APP;

KW beta-secretase; Alzheimer's disease; APP695-Sw-KK.

XX

OS Homo sapiens.

XX

FH Key Location/Qualifiers

FT Misc-difference 595

FT /note= "Wild type Lys substituted by Asn"

FT Misc-difference 596

FT /note= "Wild type Met substituted by Leu"
 XX
 PN WO200149097-A2.
 XX
 PD 12-JUL-2001.
 XX
 PF 09-MAY-2001; 2001WO-IB000797.
 XX
 PR 09-MAY-2001; 2001WO-IB000797.
 XX
 PA (BIEN/) BIENKOWSKI M J.
 PA (GURN/) GURNEY M E.
 PA (HEIN/) HEINRIKSON R L.
 PA (PARO/) PARODI L A.
 PA (YANR/) YAN R.
 XX
 PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;
 XX
 DR WPI; 2001-502548/55.
 DR N-PSDB; AAS11709.
 XX
 PT Novel purified polypeptide comprising fragment of mammalian aspartyl
 PT protease 2, lacking Asp2 transmembrane domain and retaining beta
 PT secretase activity of Asp2 useful for identifying inhibitors of Asp2
 PT activity.
 XX
 PS Example 6; Page 147-149; 185pp; English.
 XX
 CC The invention relates to a novel purified polypeptide comprising a
 CC fragment of mammalian aspartyl protease 2 (Asp2) protein which lacks the
 CC Asp2 transmembrane domain and the Asp2 protein, and where the polypeptide
 CC and the fragment retain the beta-secretase activity of the mammalian Asp2
 CC protein. Also included is an isoform of amyloid protein precursor (APP)
 CC comprising the amino acid sequence of a APP or its fragment containing an
 CC APP cleavage site recognisable by a mammalian beta-secretase, and further
 CC comprising two lysine residues at the carboxyl terminus of the amino acid
 CC sequence of the mammalian APP or APP fragment. The polypeptides are used
 CC for assaying for modulators of beta-secretase activity; identifying
 CC agents that inhibit the APP processing activity of human Asp2 aspartyl
 CC protease (Hu-Asp2); identifying agents that modulate the activity of Asp2
 CC ; and for reducing cellular production of amyloid beta (Abeta) from APP.
 CC Agents identified by the above methods are useful for treating
 CC Alzheimer's disease; and for identifying modulators of amyloid-beta
 CC (Abeta) peptide production, for use in designing therapeutics for the
 CC treatment or prevention of Alzheimer's disease. Probes and primers
 CC derived from Asp nucleic acid sequences are useful for detecting Hu-Asp
 CC nucleic acids in in vitro assays and in Northern and Southern blots. The
 CC present sequence represents the amino acid sequence of human amyloid
 CC protein precursor, APP695-Sw-KK, used in the method of the invention
 XX
 SQ Sequence 697 AA;

 Query Match 100.0%; Score 3651; DB 4; Length 697;
 Best Local Similarity 100.0%; Pred. No. 5.1e-253;
 Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAAF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAAF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMKLLKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMKLLKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK	697

RESULT 3

AAE10636

ID AAE10636 standard; protein; 697 AA.

XX

AC AAE10636;

XX

DT 10-DEC-2001 (first entry)

XX

DE Human amyloid protein precursor 695-Sw-KK (APP695-Sw-KK) isoform.

XX
KW Human; aspartyl protease 1; Aspl; amyloid precursor protein;
KW Alzheimer's disease; AD; dementia; neurofibrillary tangle; gliosis;
KW amyloid plaque; neuronal loss; proteolytic; nootropic; neuroprotective;
KW APP695-Sw-KK; mutant; mutein.
XX
OS Homo sapiens.
OS Synthetic.
XX
FH Key Location/Qualifiers
FT Misc-difference 595
FT /note= "Wild-type Lys substituted with Asn"
FT Misc-difference 596
FT /note= "Wild-type Met substituted with Leu"
XX
PN GB2357767-A.
XX
PD 04-JUL-2001.
XX
PF 22-SEP-2000; 2000GB-00023315.
XX
PR 23-SEP-1999; 99US-00404133.
PR 23-SEP-1999; 99US-0155493P.
PR 23-SEP-1999; 99WO-US020881.
PR 13-OCT-1999; 99US-00416901.
PR 06-DEC-1999; 99US-0169232P.
XX
PA (PHAA) PHARMACIA & UPJOHN CO.
XX
PI Bienkowski MJ, Gurney M;
XX
DR WPI; 2001-444208/48.
DR N-PSDB; AAD17872.
XX
PT Polypeptide comprising fragments of human aspartyl protease with amyloid
PT precursor protein processing activity and alpha-secretase activity, for
PT identifying modulators useful in treating Alzheimer's disease.
XX
PS Example 6; Page 117-119; 187pp; English.
XX
CC The patent discloses human aspartyl protease 1 (hu-Aspl) or modified Aspl
CC proteins which lack transmembrane domain or amino terminal domain or
CC cytoplasmic domain and retains alpha-secretase activity and amyloid
CC protein precursor (APP) processing activity. The proteins of the
CC invention are useful for assaying hu-Aspl alpha-secretase activity, which
CC in turn is useful for identifying modulators of hu-Aspl alpha-secretase
CC activity, where modulators that increase hu-Aspl alpha-secretase activity
CC are useful for treating Alzheimer's disease (AD) which causes progressive
CC dementia with consequent formation of amyloid plaques, neurofibrillary
CC tangles, gliosis and neuronal loss. Hu-Aspl protease substrate is useful
CC for assaying hu-Aspl proteolytic activity, by contacting hu-Aspl protein
CC with the substrate under acidic conditions and determining the level of
CC hu-Aspl proteolytic activity. The present sequence is human amyloid
CC protein precursor 695-Sw-KK (APP695-Sw-KK) isoform which is obtained by
CC the addition of two lysine residues (KK motif) at the C-terminal of
CC App695-Sw isoform which is generated by the Swedish mutation APP695,
CC where Lys at position 595 is replaced with Asn and Met at position 596 is

CC replaced with Leu. APP695-Sw-KK isoform is useful for assaying the beta-
CC secretase activity of human aspartyl protease 2a (hu-Asp2a) protein
XX
SQ Sequence 697 AA;

Query Match 100.0%; Score 3651; DB 4; Length 697;
Best Local Similarity 100.0%; Pred. No. 5.1e-253;
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    541 DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600

Qy    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
      ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
```

RESULT 4

AAE06866

ID AAE06866 standard; protein; 697 AA.

XX

AC AAE06866;

XX

DT 23-OCT-2001 (first entry)

XX

DE Human amyloid precursor protein 695-Sw-KK (APP695-Sw-KK) isoform.

XX

KW Human; aspartyl protease; Asp; beta-amyloid precursor protein 695-Sw-KK;

KW beta-secretase; Alzheimer's disease; dementia; amyloid plaque; gliosis;

KW neurofibrillary tangle; neuronal loss; amyloid-beta peptide; nootropic;

KW neuroprotective; antisense therapy; gene therapy; APP695-Sw-KK; mutant;

KW mutein.

XX

OS Homo sapiens.

OS Synthetic.

XX

FH Key Location/Qualifiers

FT Misc-difference 595

FT /note= "Wild type Lys substituted with Asn"

FT Misc-difference 596

FT /note= "Wild type Met substituted with Leu"

XX

PN WO200150829-A2.

XX

PD 19-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB000799.

XX

PR 09-MAY-2001; 2001WO-IB000799.

XX

PA (BIEN/) BIENKOWSKI M J.

PA (GURN/) GURNEY M E.

PA (HEIN/) HEINRIKSON R L.

PA (PARO/) PARODI L A.

PA (YANR/) YAN R.

XX

PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;

XX

DR WPI; 2001-483072/52.

DR N-PSDB; AAD13028.

XX

PT Novel purified polypeptide comprising fragment of mammalian aspartyl

PT protease 2, lacking Asp2 transmembrane domain and retaining beta

PT secretase activity of Asp2 useful for identifying inhibitors of Asp2

PT activity.

XX

PS Example 6; Page 147-149; 185pp; English.

XX

CC The invention relates to human aspartyl proteases (Hu-Asp), beta-amyloid

CC precursor protein (APP) isoforms and their corresponding DNA molecules.

CC Human aspartyl proteases can act as beta-secretase proteases useful for

CC treating Alzheimer's disease. APP isoforms are useful for identifying

CC modulators of amyloid-beta peptide production, for use in designing

therapeutics for the treatment and prevention of Alzheimer's disease, dementia, formation of amyloid plaques, neurofibrillary tangles, gliosis and neuronal loss. APP isoforms are also used in methods for identifying inhibitors and modulators of human Asp2 activity. The invention relates to a method for identifying agents that modulate the activity of human aspartyl protease Asp2. Amyloid-beta peptides obtained from APP are used as a means to screen in cellular assays for the inhibitors of beta- and gamma- secretase. Hu-Asp DNA fragments are useful as probes or primers in polymerase chain reactions (PCR). The probes are useful for detecting Hu-Asp nucleic acids in in vitro assays and in Northern and Southern blots. The present sequence is modified human amyloid precursor protein 695-Swedish (APP695-Sw-KK) isoform. APP695-Sw-KK isoform is obtained by addition of two Lys residues (KK motif) at the C-terminal end of APP695-Sw isoform. APP695-Sw isoform is obtained by Swedish KM-NL mutation in APP695 isoform, where Lys at position 595 is replaced with Asn, Met at position 596 is replaced with Leu. APP695-Sw-KK isoform is useful for assaying the beta-secretase activity of human aspartyl protease 2a (Hu-Asp2a) protein

XX

SQ Sequence 697 AA;

Query Match 100.0%; Score 3651; DB 4; Length 697;
 Best Local Similarity 100.0%; Pred. No. 5.1e-253;
 Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVA	480

Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
 |||
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
 |||
 Db 541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600

Qy 601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
 |||
 Db 601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
 |||
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697

RESULT 5

AAE02588

ID AAE02588 standard; protein; 697 AA.

XX

AC AAE02588;

XX

DT 10-AUG-2001 (first entry)

XX

DE Human amyloid precursor protein 695-Sw-KK (APP695-Sw-KK).

XX

KW Human; alpha-secretase; amyloid precursor protein 695-Sw-KK; therapy;

KW APP695-Sw-KK; Alzheimer's disease; antialzheimer's.

XX

OS Homo sapiens.

OS Synthetic.

XX

PN WO200123533-A2.

XX

PD 05-APR-2001.

XX

PF 22-SEP-2000; 2000WO-US026080.

XX

PR 23-SEP-1999; 99US-0155493P.

PR 23-SEP-1999; 99WO-US020881.

PR 13-OCT-1999; 99US-00416901.

PR 06-DEC-1999; 99US-0169232P.

XX

PA (PHAA) PHARMACIA & UPJOHN CO.

XX

PI Gurney M, Bienkowski MJ;

XX

DR WPI; 2001-290516/30.

DR N-PSDB; AAD06746.

XX

PT Enzymes that cleave the alpha-secretase site of the amyloid precursor protein, useful for the treatment of Alzheimer's disease.

XX

PS Example 6; Page 146-148; 189pp; English.

XX

CC The present invention relates to enzymes for cleaving the alpha-

Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697

Db 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697

RESULT 6

AAU06610

ID AAU06610 standard; protein; 697 AA.

XX

AC AAU06610;

XX

DT 24-OCT-2001 (first entry)

XX

DE Human Amyloid precursor protein mutant, APP695-SW-KK.

XX

KW Human; Aspartyl protease; Asp2b; beta-secretase; nootropic;

KW neuroprotective; amyloid protein precursor; APP; Alzheimer's disease;

KW amyloid-beta; Abeta; APP695-SW-KK; mutant; mutein.

XX

OS Homo sapiens.

XX

FH Key Location/Qualifiers

FT Misc-difference 595. .596

FT /note= "Wild-type Lys-Met substituted by Asn-Leu"

FT Misc-difference 696. .697

FT /note= "2 Extra Lys residues added compared to wild-type

FT APP695"

XX

PN WO200149098-A2.

XX

PD 12-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB000798.

XX

PR 09-MAY-2001; 2001WO-IB000798.

XX

PA (BIEN/) BIENKOWSKI M J.

PA (GURN/) GURNEY M E.

PA (HEIN/) HEINRIKSON R L.

PA (PARO/) PARODI L A.

PA (YANR/) YAN R.

XX

PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;

XX

DR WPI; 2001-502549/55.

DR N-PSDB; AAS11524.

XX

PT Novel purified polypeptide comprising fragment of mammalian aspartyl

PT protease 2, lacking Asp2 transmembrane domain and retaining beta

PT secretase activity of Asp2 useful for identifying inhibitors of Asp2

PT activity.

XX

PS Example 6; Page 147-149; 185pp; English.

XX

CC The invention relates to a purified polypeptide comprising a fragment of

CC mammalian aspartyl protease (Asp)2 protein which lacks the Asp2
 CC transmembrane domain and the Asp2 protein, and where the polypeptide and
 CC the fragment retain the beta-secretase activity of the mammalian Asp2
 CC protein. The invention also details polynucleotides for the Asp proteins
 CC and vectors expressing them, and a polypeptide (isoform of amyloid
 CC protein precursor (APP)) comprising the amino acid sequence of an APP or
 CC its fragment containing an APP cleavage site recognizable by a mammalian
 CC beta-secretase, and further comprising two lysine residues at the
 CC carboxyl terminus of the amino acid sequence of the mammalian APP or APP
 CC fragment. Also included in the invention are methods of identifying
 CC modulators or inhibitors of Asp2. Modulators and inhibitors of Asp2 are
 CC useful for treating Alzheimer's disease. APP is useful in methods for
 CC identifying inhibitors or modulators of human Asp2 activity and amyloid-
 CC beta (Abeta) peptide production. APP is also useful in designing
 CC therapeutics for the treatment or prevention of Alzheimer's disease. APP
 CC comprising the APP-Sw-beta-secretase peptide sequence (NLDA), which is
 CC associated with increased levels of Abeta processing is useful in assays
 CC relating the Alzheimer's research. The expression vector is useful for
 CC recombinantly expressing APP. Nucleic acids that hybridise to Asp
 CC oligonucleotides are useful as probes or primers. The probes are useful
 CC for detecting Hu-Asp nucleic acids in in vitro assays and in Northern and
 CC Southern blots. The present sequence is the human APP695 mutant, APP695-
 CC SW-KK which has 2 extra Lys residues added at the C-terminus compared to
 CC the APP695-SW mutant. The mutation alters the specificity of the APP
 CC gamma-secretase activity and increases the rate of processing of the
 CC amyloid Abeta peptide
 XX
 SQ Sequence 697 AA;

Query Match 100.0%; Score 3651; DB 4; Length 697;
 Best Local Similarity 100.0%; Pred. No. 5.1e-253;
 Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360

Qy	361	QEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGE	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGE	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVN	600
Db	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVN	600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQY	660
Db	601	RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQY	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK	697

RESULT 7

ABB78597

ID ABB78597 standard; protein; 697 AA.

XX

AC ABB78597;

XX

DT 16-JUL-2002 (first entry)

XX

DE Human APP695-Sw-KK protein sequence SEQ ID NO:18.

XX

KW Human; Asp-1; Asp-2; aspartyl protease; Alzheimer's disease; proteolytic;

KW amyloid precursor protein; APP.

XX

OS Homo sapiens.

XX

PN GB2367060-A.

XX

PD 27-MAR-2002.

XX

PF 29-OCT-2001; 2001GB-00025934.

XX

PR 23-SEP-1999; 99US-00404133.

PR 23-SEP-1999; 99US-0155493P.

PR 23-SEP-1999; 99WO-US020881.

PR 13-OCT-1999; 99US-00416901.

PR 06-DEC-1999; 99US-0169232P.

PR 22-SEP-2000; 2000GB-00023315.

XX

PA (PHAA) PHARMACIA & UPJOHN CO.

XX

PI Bienkowski MJ, Gurney M;

XX

DR WPI; 2002-397167/43.

DR N-PSDB; ABL52464.

XX

PT Human aspartyl protease 1 substrates useful in assays to detect aspartyl
PT protease activity, e.g. for the diagnosis of Alzheimer's disease.

XX

PS Example 6; Page 117-119; 182pp; English.

XX

CC The present invention describes a human aspartyl protease 1 (hu-Asp1)
CC substrate (I) which comprises a peptide of no more than 50 amino acids,
CC and which comprises the 8 amino acid sequence Gly-Leu-Ala-Leu-Ala-Leu-
CC Glu-Pro. Also described are: (1) a method (II) for assaying hu-Asp1
CC proteolytic activity, comprising: (a) contacting a hu-Asp1 protein with
CC (I) under acidic conditions; and (b) determining the level of hu-Asp1
CC proteolytic activity; (2) a purified polynucleotide (III) comprising a
CC nucleotide sequence that hybridises under stringent conditions to the non
CC -coding strand complementary to a defined 1804 nucleotide sequence (see
CC ABL52456) where the nucleotide sequence encodes a polypeptide having Asp1
CC proteolytic activity and lacks nucleotides encoding a transmembrane
CC domain); (3) a purified polynucleotide (III') comprising a sequence that
CC hybridises under stringent conditions to (III) (the nucleotide sequence
CC encodes a polypeptide further lacking a pro-peptide domain corresponding
CC to amino acids 23-62 of hu-Asp1 (see ABB78589)); (4) a vector (IV)
CC comprising (III) or (III'); and (5) a host cell (V) transformed or
CC transfected with (III), (III') and/or (IV). The hu-Asp1 protease
CC substrate (I) may be used as an enzyme substrate in assays to detect
CC aspartyl protease activity, (II) and therefore diagnose diseases
CC associated with aberrant hu-Asp1 expression and activity such as
CC Alzheimer's disease. Hu-Asp1 has been localised to chromosome 21, while
CC hu-Asp2 has been localised to chromosome 11q23.3-24.1. The present
CC sequence represents human amyloid precursor protein APP695-Sw-KK, which
CC is given in an example from the present invention

XX

SQ Sequence 697 AA;

Query Match 100.0%; Score 3651; DB 5; Length 697;

Best Local Similarity 100.0%; Pred. No. 5.1e-253;

Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60
          |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
          |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
          |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
          |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
          |||
```

Db 241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
 Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
 Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
 Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
 Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540
 Qy 541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEI SEVNLD AEF 600
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 Db 541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEI SEVNLD AEF 600
 Qy 601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
 ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 Db 601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
 Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
 ||||||||||||||||||||||||||||||||||||||||||||
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697

RESULT 8

AA Y88428

ID AAY88428 standard; protein; 697 AA.

XX

AC AAY88428;

XX

DT 03-AUG-2000 (first entry)

XX

DE Human APP696-KK amino acid sequence.

XX

KW Aspartyl protease; aspartase; amyloid precursor protein; APP; Asp 2;

KW Alzheimer's disease; beta secretase site; APP696-KK.

XX

OS Homo sapiens.

XX

PN WO200017369-A2.

XX

PD 30-MAR-2000.

XX

PF 23-SEP-1999; 99WO-US020881.

XX

PR 24-SEP-1998; 98US-0101594P.

XX

PA (PHAA) PHARMACIA & UPJOHN CO.

XX

PI Gurney ME, Bienkowski MJ, Heinrikson RL, Parodi LA, Yan R;

Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFS	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFS	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGHV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGHV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMOONGYENPTYKFFEOMONKK	697

PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;
XX
DR WPI; 2001-502548/55.
DR N-PSDB; AAS11708.
XX
PT Novel purified polypeptide comprising fragment of mammalian aspartyl
PT protease 2, lacking Asp2 transmembrane domain and retaining beta
PT secretase activity of Asp2 useful for identifying inhibitors of Asp2
PT activity.

XX
PS Example 6; Page 144-146; 185pp; English.
XX

CC The invention relates to a novel purified polypeptide comprising a
CC fragment of mammalian aspartyl protease 2 (Asp2) protein which lacks the
CC Asp2 transmembrane domain and the Asp2 protein, and where the polypeptide
CC and the fragment retain the beta-secretase activity of the mammalian Asp2
CC protein. Also included is an isoform of amyloid protein precursor (APP)
CC comprising the amino acid sequence of a APP or its fragment containing an
CC APP cleavage site recognisable by a mammalian beta-secretase, and further
CC comprising two lysine residues at the carboxyl terminus of the amino acid
CC sequence of the mammalian APP or APP fragment. The polypeptides are used
CC for assaying for modulators of beta-secretase activity; identifying
CC agents that inhibit the APP processing activity of human Asp2 aspartyl
CC protease (Hu-Asp2); identifying agents that modulate the activity of Asp2
CC ; and for reducing cellular production of amyloid beta (Abeta) from APP.
CC Agents identified by the above methods are useful for treating
CC Alzheimer's disease; and for identifying modulators of amyloid-beta
CC (Abeta) peptide production, for use in designing therapeutics for the
CC treatment or prevention of Alzheimer's disease. Probes and primers
CC derived from Asp nucleic acid sequences are useful for detecting Hu-Asp
CC nucleic acids in in vitro assays and in Northern and Southern blots. The
CC present sequence represents the amino acid sequence of human amyloid
CC protein precursor, APP695-KK, used in the method of the invention

XX
SQ Sequence 697 AA;

Query Match 99.8%; Score 3643; DB 4; Length 697;
Best Local Similarity 99.7%; Pred. No. 1.9e-252;
Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHNMNVQNGKWDSDPSGTK 60
|
Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHNMNVQNGKWDSDPSGTK 60

Qy 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIRCLVG 120
|
Db 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIRCLVG 120

Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
|
Db 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy 181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
|
Db 181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

Qy 241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Db	241	EADDDDEDDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 10

AAE10635

ID AAE10635 standard; protein; 697 AA.

XX

AC AAE10635;

XX

DT 10-DEC-2001 (first entry)

XX

DE Human amyloid protein precursor 695-KK (APP695-KK) isoform.

XX

KW Human; aspartyl protease 1; Aspl; amyloid precursor protein; APP695-KK;

KW Alzheimer's disease; AD; dementia; neurofibrillary tangle; gliosis;

KW amyloid plaque; neuronal loss; proteolytic; nootropic; neuroprotective.

XX

OS Homo sapiens.

OS Synthetic.

XX

PN GB2357767-A.

XX

PD 04-JUL-2001.

XX

PF 22-SEP-2000; 2000GB-00023315.

XX

PR 23-SEP-1999; 99US-00404133.

PR 23-SEP-1999; 99US-0155493P.

PR 23-SEP-1999; 99WO-US020881.
PR 13-OCT-1999; 99US-00416901.
PR 06-DEC-1999; 99US-0169232P.

XX

PA (PHAA) PHARMACIA & UPJOHN CO.

XX

PI Bienkowski MJ, Gurney M;

XX

DR WPI; 2001-444208/48.

DR N-PSDB; AAD17871.

XX

PT Polypeptide comprising fragments of human aspartyl protease with amyloid
PT precursor protein processing activity and alpha-secretase activity, for
PT identifying modulators useful in treating Alzheimer's disease.

XX

PS Example 6; Page 114-116; 187pp; English.

XX

CC The patent discloses human aspartyl protease 1 (hu-Asp1) or modified Asp1
CC proteins which lack transmembrane domain or amino terminal domain or
CC cytoplasmic domain and retains alpha-secretase activity and amyloid
CC protein precursor (APP) processing activity. The proteins of the
CC invention are useful for assaying hu-Asp1 alpha-secretase activity, which
CC in turn is useful for identifying modulators of hu-Asp1 alpha-secretase
CC activity, where modulators that increase hu-Asp1 alpha-secretase activity
CC are useful for treating Alzheimer's disease (AD) which causes progressive
CC dementia with consequent formation of amyloid plaques, neurofibrillary
CC tangles, gliosis and neuronal loss. Hu-Asp1 protease substrate is useful
CC for assaying hu-Asp1 proteolytic activity, by contacting hu-Asp1 protein
CC with the substrate under acidic conditions and determining the level of
CC hu-Asp1 proteolytic activity. The present sequence is human amyloid
CC protein precursor 695-KK (APP695-KK) isoform which is obtained by the
CC addition of two Lys residues (KK motif) at the C-terminus of APP695
CC protein

XX

SQ Sequence 697 AA;

Query Match 99.8%; Score 3643; DB 4; Length 697;
Best Local Similarity 99.7%; Pred. No. 1.9e-252;
Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60
|
Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60

Qy 61 TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
|
Db 61 TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
|
Db 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy 181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
|
Db 181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

Qy 241 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Db	241	 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAAF	600
Db	541	 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAAF	600
Qy	601	RHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKKQYTSIHGGV	660
Db	601	 RHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 11

AAE06865

ID AAE06865 standard; protein; 697 AA.

XX

AC AAE06865;

XX

DT 23-OCT-2001 (first entry)

XX

DE Human amyloid precursor protein 695-KK (APP695-KK) isoform.

XX

KW Human; aspartyl protease; Asp; beta-amyloid precursor protein 695-KK;
KW beta-secretase; Alzheimer's disease; dementia; amyloid plaque; gliosis;
KW neurofibrillary tangle; neuronal loss; amyloid-beta peptide; nootropic;
KW neuroprotective; antisense therapy; gene therapy; APP695-KK; mutant;
KW mutein.

XX

OS Homo sapiens.

XX

PN WO200150829-A2.

XX

PD 19-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB000799.

XX

PR 09-MAY-2001; 2001WO-IB000799.

XX
PA (BIEN/) BIENKOWSKI M J.
PA (GURN/) GURNEY M E.
PA (HEIN/) HEINRIKSON R L.
PA (PARO/) PARODI L A.
PA (YANR/) YAN R.
XX
PI Bienkowski MJ, Gurney ME, Heinrikson RL, Parodi LA, Yan R;
XX
DR WPI; 2001-483072/52.
DR N-PSDB; AAD13027.
XX
PT Novel purified polypeptide comprising fragment of mammalian aspartyl
PT protease 2, lacking Asp2 transmembrane domain and retaining beta
PT secretase activity of Asp2 useful for identifying inhibitors of Asp2
PT activity.
XX
PS Example 6; Page 144-146; 185pp; English.
XX
CC The invention relates to human aspartyl proteases (Hu-Asp), beta-amyloid
CC precursor protein (APP) isoforms and their corresponding DNA molecules.
CC Human aspartyl proteases can act as beta-secretase proteases useful for
CC treating Alzheimer's disease. APP isoforms are useful for identifying
CC modulators of amyloid-beta peptide production, for use in designing
CC therapeutics for the treatment and prevention of Alzheimer's disease,
CC dementia, formation of amyloid plaques, neurofibrillary tangles, gliosis
CC and neuronal loss. APP isoforms are also used in methods for identifying
CC inhibitors and modulators of human Asp2 activity. The invention relates
CC to a method for identifying agents that modulate the activity of human
CC aspartyl protease Asp2. Amyloid-beta peptides obtained from APP are used
CC as a means to screen in cellular assays for the inhibitors of beta- and
CC gamma- secretase. Hu-Asp DNA fragments are useful as probes or primers in
CC polymerase chain reactions (PCR). The probes are useful for detecting Hu-
CC Asp nucleic acids in in vitro assays and in Northern and Southern blots.
CC The present sequence is modified human amyloid precursor protein 695-KK
CC (APP695-KK) isoform. APP695-KK isoform is obtained by addition of two Lys
CC residues (KK motif) at the C-terminal end of APP695 isoform
XX
SQ Sequence 697 AA;

Query Match 99.8%; Score 3643; DB 4; Length 697;
Best Local Similarity 99.7%; Pred. No. 1.9e-252;
Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSG	TK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSG	TK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI	PYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI	PYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDK	KFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDK	KFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEE		240

Db	181		240
Qy	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241		300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301		360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361		420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421		480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481		540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNDAEF	600
Db	541		600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMMLKKKQYTSIHHGV	660
Db	601		660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661		697

RESULT 12

AAE02587

ID AAE02587 standard; protein; 697 AA.

XX

AC AAE02587;

XX

DT 10-AUG-2001 (first entry)

XX

DE Human amyloid precursor protein 695-KK (APP695-KK).

XX

KW Human; alpha-secretase; amyloid precursor protein 695-KK; APP695-KK;
therapy; Alzheimer's disease; antialzheimer's.

XX

OS Homo sapiens.

OS Synthetic.

XX

PN WO200123533-A2.

XX

PD 05-APR-2001.

XX

PF 22-SEP-2000; 2000WO-US026080.


```

Db      361  |||||
Qy      421  KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
Db      421  |||||
Qy      481  EEIQDEVDELLQKEQNYSDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSL 540
Db      481  |||||
Qy      541  DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
Db      541  |||||
Qy      601  RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HGV 660
Db      601  |||||
Qy      661  VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
Db      661  |||||

```

RESULT 13

AAU06609

ID AAU06609 standard; protein; 697 AA.

XX

AC AAU06609;

XX

DT 24-OCT-2001 (first entry)

XX

DE Human Amyloid precursor protein mutant, APP695-KK.

XX

KW Human; Aspartyl protease; Asp2b; beta-secretase; nootropic;

KW neuroprotective; amyloid protein precursor; APP; Alzheimer's disease;

KW amyloid-beta; Abeta; APP695-KK; mutant; mutein.

XX

OS Homo sapiens.

XX

FH Key Location/Qualifiers

FT Misc-difference 696. .697

FT /note= "2 Extra Lys residues added compared to wild-type
APP695"

XX

PN WO200149098-A2.

XX

PD 12-JUL-2001.

XX

PF 09-MAY-2001; 2001WO-IB000798.

XX

PR 09-MAY-2001; 2001WO-IB000798.

XX

PA (BIEN/) BIENKOWSKI M J.

PA (GURN/) GURNEY M E.

PA (HEIN/) HEINRIKSON R L.

PA (PARO/) PARODI L A.

XX

XX

DR

XX

XX

XX

CC

XX

Query Match

99.8%; Score 3643; DB 4; Length 697;

Best Local Similarity 99.7%; Pred. No. 1.9e-252;

Matches 695: Conservative 1: Mismatches 1: Indels 0: Gaps 0:

Ov

Db

Ov

Db

Ov

Db	121	 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNDAEF	600
Db	541	 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Db	601	 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK	697
Db	661	 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK	697

RESULT 14

ABB78596

ID ABB78596 standard; protein; 697 AA.

XX

AC ABB78596;

XX

DT 16-JUL-2002 (first entry)

XX

DE Human APP695-KK protein sequence SEQ ID NO:16.

XX

KW Human; Asp-1; Asp-2; aspartyl protease; Alzheimer's disease; proteolytic;
KW amyloid precursor protein; APP.

XX

OS Homo sapiens.

XX

PN GB2367060-A.

XX

PD 27-MAR-2002.

XX

PF 29-OCT-2001; 2001GB-00025934.

XX

PR 23-SEP-1999; 99US-00404133.

PR 23-SEP-1999; 99US-0155493P.

PR 23-SEP-1999; 99WO-US020881.

PR 13-OCT-1999; 99US-00416901.

PR 06-DEC-1999; 99US-0169232P.

PR 22-SEP-2000; 2000GB-00023315.

XX

PA (PHAA) PHARMACIA & UPJOHN CO.

XX

PI Bienkowski MJ, Gurney M;

XX

DR WPI; 2002-397167/43.

DR N-PSDB; ABL52463.

XX

PT Human aspartyl protease 1 substrates useful in assays to detect aspartyl
PT protease activity, e.g. for the diagnosis of Alzheimer's disease.

XX

PS Example 6; Page 114-116; 182pp; English.

XX

CC The present invention describes a human aspartyl protease 1 (hu-Asp1)
CC substrate (I) which comprises a peptide of no more than 50 amino acids,
CC and which comprises the 8 amino acid sequence Gly-Leu-Ala-Leu-Ala-Leu-
CC Glu-Pro. Also described are: (1) a method (II) for assaying hu-Asp1
CC proteolytic activity, comprising: (a) contacting a hu-Asp1 protein with
CC (I) under acidic conditions; and (b) determining the level of hu-Asp1
CC proteolytic activity; (2) a purified polynucleotide (III) comprising a
CC nucleotide sequence that hybridises under stringent conditions to the non
CC -coding strand complementary to a defined 1804 nucleotide sequence (see
CC ABL52456) where the nucleotide sequence encodes a polypeptide having Asp1
CC proteolytic activity and lacks nucleotides encoding a transmembrane
CC domain); (3) a purified polynucleotide (III') comprising a sequence that
CC hybridises under stringent conditions to (III) (the nucleotide sequence
CC encodes a polypeptide further lacking a pro-peptide domain corresponding
CC to amino acids 23-62 of hu-Asp1 (see ABB78589)); (4) a vector (IV)
CC comprising (III) or (III'); and (5) a host cell (V) transformed or
CC transfected with (III), (III') and/or (IV). The hu-Asp1 protease
CC substrate (I) may be used as an enzyme substrate in assays to detect
CC aspartyl protease activity, (II) and therefore diagnose diseases
CC associated with aberrant hu-Asp1 expression and activity such as
CC Alzheimer's disease. Hu-Asp1 has been localised to chromosome 21, while
CC hu-Asp2 has been localised to chromosome 11q23.3-24.1. The present
CC sequence represents human amyloid precursor protein APP695-KK, which is
CC given in an example from the present invention

XX

SQ Sequence 697 AA;

Query Match 99.8%; Score 3643; DB 5; Length 697;

Best Local Similarity 99.7%; Pred. No. 1.9e-252;

Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

|||||

Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 15

AA Y88435

ID AAY88435 standard; protein; 695 AA.

XX

AC AAY88435;

XX

DT 03-AUG-2000 (first entry)

XX

DE Human APP695-sw variant amino acid sequence.

XX

KW Aspartyl protease; aspartase; amyloid precursor protein; APP; Asp 2;

Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDEDGDEVEEEAEEPYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDEDGDEVEEEAEEPYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDDLANMISEPRISYGNALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDADF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDADF	600
Qy	601	RHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Db	601	RHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695

Search completed: July 26, 2004, 12:44:00
Job time : 51.3333 secs

GenCore version 5.1.6
Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:41:23 ; Search time 15 Seconds
(without alignments)
2398.887 Million cell updates/sec

Title: US-09-806-194A-18
Perfect score: 3651
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 389414 seqs, 51625971 residues

Total number of hits satisfying chosen parameters: 389414

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : Issued_Patents_AA:*
1: /cgn2_6/ptodata/2/iaa/5A_COMB.pep:*
2: /cgn2_6/ptodata/2/iaa/5B_COMB.pep:*
3: /cgn2_6/ptodata/2/iaa/6A_COMB.pep:*
4: /cgn2_6/ptodata/2/iaa/6B_COMB.pep:*
5: /cgn2_6/ptodata/2/iaa/PCTUS_COMB.pep:*
6: /cgn2_6/ptodata/2/iaa/backfiles1.pep:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	%		DB	ID	Description
		Query Match	Length			
1	3651	100.0	697	4	US-09-548-372D-18	Sequence 18, Appl
2	3651	100.0	697	4	US-09-548-367D-18	Sequence 18, Appl
3	3651	100.0	697	4	US-09-551-853D-18	Sequence 18, Appl
4	3643	99.8	697	4	US-09-548-372D-16	Sequence 16, Appl
5	3643	99.8	697	4	US-09-548-367D-16	Sequence 16, Appl
6	3643	99.8	697	4	US-09-551-853D-16	Sequence 16, Appl
7	3641	99.7	695	4	US-09-548-372D-12	Sequence 12, Appl
8	3641	99.7	695	4	US-09-548-367D-12	Sequence 12, Appl
9	3641	99.7	695	4	US-09-551-853D-12	Sequence 12, Appl
10	3638	99.6	697	4	US-09-548-372D-20	Sequence 20, Appl
11	3638	99.6	697	4	US-09-548-367D-20	Sequence 20, Appl

12	3638	99.6	697	4	US-09-551-853D-20	Sequence 20, Appl
13	3633	99.5	695	1	US-08-123-702-2	Sequence 2, Appli
14	3633	99.5	695	2	US-08-104-165-1	Sequence 1, Appli
15	3633	99.5	695	3	US-08-464-250-1	Sequence 1, Appli
16	3633	99.5	695	4	US-08-464-250-1	Sequence 1, Appli
17	3633	99.5	695	4	US-09-458-481B-7	Sequence 7, Appli
18	3633	99.5	695	4	US-09-458-481B-8	Sequence 8, Appli
19	3633	99.5	695	4	US-09-548-372D-10	Sequence 10, Appl
20	3633	99.5	695	4	US-09-548-367D-10	Sequence 10, Appl
21	3633	99.5	695	4	US-09-551-853D-10	Sequence 10, Appl
22	3633	99.5	695	4	US-09-415-099-6	Sequence 6, Appli
23	3633	99.5	695	6	5218100-2	Patent No. 5218100
24	3628	99.4	695	4	US-09-548-372D-14	Sequence 14, Appl
25	3628	99.4	695	4	US-09-548-367D-14	Sequence 14, Appl
26	3628	99.4	695	4	US-09-551-853D-14	Sequence 14, Appl
27	3627	99.3	694	1	US-08-339-152A-18	Sequence 18, Appl
28	3627	99.3	694	2	US-08-007-999B-5	Sequence 5, Appli
29	3627	99.3	694	2	US-08-689-276A-5	Sequence 5, Appli
30	3621	99.2	695	1	US-08-371-930-27	Sequence 27, Appl
31	3621	99.2	695	5	PCT-US94-01712-27	Sequence 27, Appl
32	3609	98.8	695	1	US-08-339-152A-30	Sequence 30, Appl
33	3604	98.7	753	4	US-09-548-372D-61	Sequence 61, Appl
34	3604	98.7	753	4	US-09-548-367D-61	Sequence 61, Appl
35	3604	98.7	753	4	US-09-551-853D-61	Sequence 61, Appl
36	3594	98.4	751	1	US-08-123-702-4	Sequence 4, Appli
37	3594	98.4	751	2	US-08-104-165-2	Sequence 2, Appli
38	3594	98.4	751	2	US-08-422-333-2	Sequence 2, Appli
39	3594	98.4	751	2	US-08-422-333-21	Sequence 21, Appl
40	3594	98.4	751	3	US-08-464-250-2	Sequence 2, Appli
41	3594	98.4	751	4	US-08-464-250-2	Sequence 2, Appli
42	3594	98.4	751	4	US-08-832-867-5	Sequence 5, Appli
43	3594	98.4	751	4	US-09-548-372D-57	Sequence 57, Appl
44	3594	98.4	751	4	US-09-548-367D-57	Sequence 57, Appl
45	3594	98.4	751	4	US-09-551-853D-57	Sequence 57, Appl

ALIGNMENTS

RESULT 1

US-09-548-372D-18

; Sequence 18, Application US/09548372D

; Patent No. 6420534

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280I

; CURRENT APPLICATION NUMBER: US/09/548,372D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 18
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-548-372D-18

Query Match 100.0%; Score 3651; DB 4; Length 697;
Best Local Similarity 100.0%; Pred. No. 4.6e-268;
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVPIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVPIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEATERTTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEATERTTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDGDGEVEEEAEEPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDGDGEVEEEAEEPYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV	300

Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
 |||
 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
 |||
 Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVA 480
 |||
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFS 540
 |||
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFS 540

Qy 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD 600
 |||
 Db 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH 660
 |||
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
 |||
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

RESULT 3

US-09-551-853D-18

; Sequence 18, Application US/09551853D

; Patent No. 6500667

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280L

; CURRENT APPLICATION NUMBER: US/09/551,853D

; CURRENT FILING DATE: 2000-04-18

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 18

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-551-853D-18

Query Match 100.0%; Score 3651; DB 4; Length 697;
Best Local Similarity 100.0%; Pred. No. 4.6e-268;
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNDAEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNDAEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLMLKKKQYTSIHGCV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLMLKKKQYTSIHGCV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 4
US-09-548-372D-16
; Sequence 16, Application US/09548372D

```

; Patent No. 6420534
; GENERAL INFORMATION:
; APPLICANT: GURNEY ET AL.
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280I
; CURRENT APPLICATION NUMBER: US/09/548,372D
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 16
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-548-372D-16

```

```

Query Match          99.8%; Score 3643; DB 4; Length 697;
Best Local Similarity 99.7%; Pred. No. 1.9e-267;
Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

```

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
|
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
|
Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
|
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
|
Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
|
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
|
Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
|
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
|
Qy    241 EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
|
Db    241 EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
|
Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
|
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
|
Qy    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
|
Db    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

```

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
 |||
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540
 |||
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
 ||| :|||
 Db 541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
 |||
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
 |||
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697

RESULT 5

US-09-548-367D-16

; Sequence 16, Application US/09548367D

; Patent No. 6440698

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280H

; CURRENT APPLICATION NUMBER: US/09/548,367D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 16

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-548-367D-16

Query Match 99.8%; Score 3643; DB 4; Length 697;

Best Local Similarity 99.7%; Pred. No. 1.9e-267;

Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
 |||

Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
		:	
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697

RESULT 6

US-09-551-853D-16

; Sequence 16, Application US/09551853D

; Patent No. 6500667

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280L

; CURRENT APPLICATION NUMBER: US/09/551,853D

; CURRENT FILING DATE: 2000-04-18

; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 16
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-551-853D-16

Query Match 99.8%; Score 3643; DB 4; Length 697;
Best Local Similarity 99.7%; Pred. No. 1.9e-267;
Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEEEE	240
Qy	241	EADDDDEDGDEVEEEAEEPVEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEEPVEEATERTTSIATTTTTTTSVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600

```

Db      541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600
Qy      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660
Db      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660
Qy      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
Db      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

```

RESULT 7

US-09-548-372D-12

; Sequence 12, Application US/09548372D

; Patent No. 6420534

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280I

; CURRENT APPLICATION NUMBER: US/09/548,372D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 12

; LENGTH: 695

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-548-372D-12

Query Match 99.7%; Score 3641; DB 4; Length 695;

Best Local Similarity 100.0%; Pred. No. 2.6e-267;

Matches 695; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60
Qy      61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
Db      61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
Qy      121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
Db      121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
Qy      181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

```


Db	181		240
Qy	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241		300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301		360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361		420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421		480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481		540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Db	541		600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HGV	660
Db	601		660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	661		695

RESULT 8

US-09-548-367D-12

; Sequence 12, Application US/09548367D

; Patent No. 6440698

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280H

; CURRENT APPLICATION NUMBER: US/09/548,367D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 12
; LENGTH: 695
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-548-367D-12

Query Match 99.7%; Score 3641; DB 4; Length 695;
Best Local Similarity 100.0%; Pred. No. 2.6e-267;
Matches 695; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEI SEVNLD AEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEI SEVNLD AEF	600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QN	695

RESULT 9

US-09-551-853D-12

; Sequence 12, Application US/09551853D

; Patent No. 6500667

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280L

; CURRENT APPLICATION NUMBER: US/09/551,853D

; CURRENT FILING DATE: 2000-04-18

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 12

; LENGTH: 695

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-551-853D-12

Query Match 99.7%; Score 3641; DB 4; Length 695;

Best Local Similarity 100.0%; Pred. No. 2.6e-267;

Matches 695; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        |||

```

Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHG V	660
Db	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHG V	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695

US-09-548-372D-20

; Patent No. 6420534

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES

; FILE REFERENCE: 29915/6280I

; CURRENT APPLICATION NUMBER: US/09/548,372D

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEO ID NOS: 73

```
; SOFTWARE: PatentIn version 3.1
```

; SEO ID NO 20

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-548-372D-20

Best Local Similarity 99.6%; Pred. No. 4.4e-267;

Matches 694; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEEEE 240
      |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEEEE 240

Qy    241 EADDDDEDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
      |||
Db    241 EADDDDEDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF 360
      |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
      |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
      |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL 540
      |||
Db    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
      |||
Db    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF 600

Qy    601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITL VMLKKKQYTSI HHGV 660
      |||
Db    601 RHDSGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIFITL VMLKKKQYTSI HHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
      |||
Db    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697

```

RESULT 11

US-09-548-367D-20

; Sequence 20, Application US/09548367D

; Patent No. 6440698

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

```

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR
AND USES
; TITLE OF INVENTION: THEREOF
; FILE REFERENCE: 29915/6280H
; CURRENT APPLICATION NUMBER: US/09/548,367D
; CURRENT FILING DATE: 2000-04-12
; PRIOR APPLICATION NUMBER: US 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: US 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn version 3.1
; SEQ ID NO 20
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-548-367D-20

```

```

Query Match          99.6%; Score 3638; DB 4; Length 697;
Best Local Similarity 99.6%; Pred. No. 4.4e-267;
Matches 694; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

```

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

```

```

Qy      481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL 540
        |||
Db      481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL 540

Qy      541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
        |||
Db      541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF 600

Qy      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH HGV 660
        |||
Db      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIH HGV 660

Qy      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
        |||
Db      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697

```

RESULT 12

US-09-551-853D-20

; Sequence 20, Application US/09551853D

; Patent No. 6500667

; GENERAL INFORMATION:

; APPLICANT: GURNEY ET AL.

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR AND USES

; TITLE OF INVENTION: THEREOF

; FILE REFERENCE: 29915/6280L

; CURRENT APPLICATION NUMBER: US/09/551,853D

; CURRENT FILING DATE: 2000-04-18

; PRIOR APPLICATION NUMBER: US 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: US 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn version 3.1

; SEQ ID NO 20

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-551-853D-20

Query Match 99.6%; Score 3638; DB 4; Length 697;

Best Local Similarity 99.6%; Pred. No. 4.4e-267;

Matches 694; Conservative 1; Mismatches 2; Indels 0; Gaps 0;

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSG TK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSG TK 60

Qy      61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db      61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

```

Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
		:	
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIFITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697

RESULT 13

US-08-123-702-2

; Sequence 2, Application US/08123702

; Patent No. 5604131

; GENERAL INFORMATION:

; APPLICANT: Wadsworth, Samuel

; APPLICANT: Snyder, Benjamin

; APPLICANT: Reddy, Vermuri, B.

; APPLICANT: Wei, Chamer

; TITLE OF INVENTION: A cDNA Genomic Hybrid Sequence Encoding APP770

; Patent No. 5604131

; TITLE OF INVENTION: Containing a Genomic DNA Insert of the KI and OX-2 Regions

; NUMBER OF SEQUENCES: 45

; CORRESPONDENCE ADDRESS:


```

;      ADDRESSEE:  Patrea L. Pabst
;      STREET:    2800 One Atlantic Center
;      STREET:    1201 West Peachtree Street
;      CITY:      Atlanta
;      STATE:     GA
;      COUNTRY:   USA
;      ZIP:       30309-3450
;      COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:   IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:   PatentIn Release #1.0, Version #1.25
;      CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/123,702
;      FILING DATE:    17-SEPT-1993
;      CLASSIFICATION:  435
;      ATTORNEY/AGENT INFORMATION:
;      NAME:         Pabst, Patrea L.
;      REGISTRATION NUMBER:  31,284
;      REFERENCE/DOCKET NUMBER:  TSI121
;      TELECOMMUNICATION INFORMATION:
;      TELEPHONE:    (404)-873-8794
;      TELEFAX:     (404)-873-8795
;      INFORMATION FOR SEQ ID NO:  2:
;      SEQUENCE CHARACTERISTICS:
;      LENGTH:       695 amino acids
;      TYPE:          amino acid
;      TOPOLOGY:     linear
;      MOLECULE TYPE:  protein
US-08-123-702-2

```

```

Query Match          99.5%;  Score 3633;  DB 1;  Length 695;
Best Local Similarity 99.7%;  Pred. No. 1.1e-266;
Matches 693;  Conservative 1;  Mismatches 1;  Indels 0;  Gaps 0;

```

```

Qy      1  MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1  MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61  TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61  TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121  EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121  EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181  GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181  GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241  EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241  EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301  DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
        |||

```

Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
 |||

Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480
 |||

Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540
 |||

Db 481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
 ||| :|||

Db 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF 600

Qy 601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
 |||

Db 601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
 |||

Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695

RESULT 14

US-08-104-165-1

; Sequence 1, Application US/08104165

; Patent No. 5877015

; GENERAL INFORMATION:

; APPLICANT: HARDY, John Anthony

; APPLICANT: GOATE, Alison Mary

; APPLICANT: MULLAN, Michael John

; APPLICANT: CHARTIER-HARLIN, Marie-Christine

; APPLICANT: OWEN, Michael John

; TITLE OF INVENTION: Test and Model for Alzheimer's Disease

; NUMBER OF SEQUENCES: 44

; CORRESPONDENCE ADDRESS:

; ADDRESSEE: Townsend and Townsend Khourie and Crew

; STREET: 379 Lytton Avenue

; CITY: Palo Alto

; STATE: California

; COUNTRY: US

; ZIP: 94301

; COMPUTER READABLE FORM:

; MEDIUM TYPE: Floppy Disk

; COMPUTER: IBM PC compatible

; OPERATING SYSTEM: PC-DOS/MS-DOS

; CURRENT APPLICATION DATA:

; APPLICATION NUMBER: US/08/104,165

; FILING DATE: 21-JAN-1992

; CLASSIFICATION: 435

; PRIOR APPLICATION DATA:

; APPLICATION NUMBER: 9101307.8

; FILING DATE: 21-JAN-1991

```

; APPLICATION NUMBER: 9118445.7
; FILING DATE: 28-AUG-1991
; ATTORNEY/AGENT INFORMATION:
; NAME: Liebeschuetz, Joe
; REGISTRATION NUMBER: 37,505
; REFERENCE/DOCKET NUMBER: 16163-000100
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (415) 326-2400
; TELEFAX: (415) 326-2422
; INFORMATION FOR SEQ ID NO: 1:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 695 amino acids
; TYPE: amino acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; MOLECULE TYPE: protein
US-08-104-165-1

```

```

Query Match          99.5%; Score 3633; DB 2; Length 695;
Best Local Similarity 99.7%; Pred. No. 1.1e-266;
Matches 693; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

```

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFS 540
        |||
Db    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFS 540

```

Qy 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
 ||| :|||
 Db 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVM LKKKQYTSIH HGV 660
 ||| :|||
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVM LKKKQYTSIH HGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFE QMQN 695
 ||| :|||
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFE QMQN 695

RESULT 15

US-08-464-250-1

; Sequence 1, Application US/08464250

; Patent No. 6107542

; GENERAL INFORMATION:

; APPLICANT: HARDY, John Anthony

; APPLICANT: GOATE, Alison Mary

; APPLICANT: MULLAN, Michael John

; APPLICANT: CHARTIER-HARLIN, Marie-Christine

; APPLICANT: OWEN, Michael John

; TITLE OF INVENTION: Test and Model for Alzheimer's Disease

; NUMBER OF SEQUENCES: 44

; CORRESPONDENCE ADDRESS:

; ADDRESSEE: Townsend and Townsend Khourie and Crew

; STREET: 379 Lytton Avenue

; CITY: Palo Alto

; STATE: California

; COUNTRY: US

; ZIP: 94301

; COMPUTER READABLE FORM:

; MEDIUM TYPE: Floppy Disk

; COMPUTER: IBM PC compatible

; OPERATING SYSTEM: PC-DOS/MS-DOS

; CURRENT APPLICATION DATA:

; APPLICATION NUMBER: US/08/464,250

; FILING DATE: 05-JUN-1995

; CLASSIFICATION: 435

; PRIOR APPLICATION DATA:

; APPLICATION NUMBER: 08/104,165

; FILING DATE: 21-JAN-1992

; APPLICATION NUMBER: 9101307.8

; FILING DATE: 21-JAN-1991

; APPLICATION NUMBER: 9118445.7

; FILING DATE: 28-AUG-1991

; ATTORNEY/AGENT INFORMATION:

; NAME: Liebeschuetz, Joe

; REGISTRATION NUMBER: 37,505

; REFERENCE/DOCKET NUMBER: 16163-000100

; TELECOMMUNICATION INFORMATION:

; TELEPHONE: (415) 326-2400

; TELEFAX: (415) 326-2422

; INFORMATION FOR SEQ ID NO: 1:

; SEQUENCE CHARACTERISTICS:

; LENGTH: 695 amino acids
; TYPE: amino acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; MOLECULE TYPE: protein
US-08-464-250-1

Query Match 99.5%; Score 3633; DB 3; Length 695;
Best Local Similarity 99.7%; Pred. No. 1.1e-266;
Matches 693; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
        |||
Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
        |||
Db    541 DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
        |||
Db    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
        |||
```

Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695

Search completed: July 26, 2004, 12:48:21
Job time : 16 secs

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:40:23 ; Search time 13.6667 Seconds
(without alignments)
4905.768 Million cell updates/sec

Title: US-09-806-194A-18
Perfect score: 3651
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 283366 seqs, 96191526 residues

Total number of hits satisfying chosen parameters: 283366

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : PIR_78:*
1: pir1:*
2: pir2:*
3: pir3:*
4: pir4:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	% Query		Length	DB	ID	Description
	Score	Match				
1	3633	99.5	695	1	A49795	Alzheimer's diseas
2	3582.5	98.1	770	1	QRHUA4	Alzheimer's diseas
3	3536	96.9	695	2	S00550	Alzheimer's diseas
4	3511	96.2	695	2	A27485	Alzheimer's diseas
5	3095	84.8	747	2	JH0773	Alzheimer's diseas
6	2105	57.7	484	4	A32761	hypothetical Alzhe
7	1725	47.2	763	2	A49321	amyloid beta (A4)
8	1709	46.8	765	2	S42880	amyloid precursor-
9	1699	46.5	751	2	A49974	beta-amyloid precu
10	1183	32.4	653	2	A46362	amyloid precursor-
11	1138	31.2	511	2	JC1404	CDEI-box DNA-bindi
12	815.5	22.3	686	2	T15795	hypothetical prote
13	746	20.4	886	2	A32758	beta-amyloid-like

14	706	19.3	246	2	S38344	CDEI-binding prote
15	403	11.0	82	2	PQ0438	Alzheimer's diseas
16	289.5	7.9	191	2	A35981	sperm membrane pro
17	275	7.5	57	2	E60045	Alzheimer's diseas
18	275	7.5	57	2	F60045	Alzheimer's diseas
19	275	7.5	57	2	G60045	Alzheimer's diseas
20	275	7.5	57	2	D60045	Alzheimer's diseas
21	275	7.5	57	2	A60045	Alzheimer's diseas
22	275	7.5	57	2	B60045	Alzheimer's diseas
23	217	5.9	42	2	PN0512	beta-amyloid prote
24	192.5	5.3	1110	2	I51116	NF-180 - sea lampr
25	186	5.1	5170	2	T15348	hypothetical prote
26	185.5	5.1	407	1	EDBEQ3	immediate-early pr
27	185.5	5.1	993	2	S49461	synaptonemal compl
28	182	5.0	522	2	T32444	hypothetical prote
29	175.5	4.8	802	1	S48529	NAB3 protein - yea
30	175.5	4.8	1188	2	T46608	zinc finger protei
31	174	4.8	579	2	JH0820	160K golgi antigen
32	174	4.8	1087	2	T30330	gelsolin-related p
33	172	4.7	675	2	T03744	myoD protein inhib
34	172	4.7	784	2	PN0009	neurofilament trip
35	172	4.7	1182	2	T30189	myelin transcripti
36	171.5	4.7	793	1	JH0628	caldesmon - human
37	171.5	4.7	884	2	T20405	hypothetical prote
38	171.5	4.7	885	2	G71608	ATP-dept. acyl-CoA
39	171	4.7	1271	2	A45555	glutamate rich pro
40	170	4.7	464	2	H90279	microtubule bindin
41	170	4.7	1948	2	S00485	gene 11-1 protein
42	169.5	4.6	298	1	TPHUTC	troponin T, cardia
43	169.5	4.6	1875	2	S38173	myosin-like protei
44	169	4.6	771	1	A33430	h-caldesmon - chic
45	169	4.6	1187	2	T46637	transcription fact

ALIGNMENTS

RESULT 1

A49795

Alzheimer's disease amyloid beta protein precursor - crab-eating macaque

C;Species: *Macaca fascicularis* (crab-eating macaque)

C;Date: 10-Sep-1999 #sequence_revision 10-Sep-1999 #text_change 10-Sep-1999

C;Accession: A49795

R;Podlisny, M.B.; Tolan, D.R.; Selkoe, D.J.

Am. J. Pathol. 138, 1423-1435, 1991

A;Title: Homology of the amyloid beta protein precursor in monkey and human supports a primate model for beta amyloidosis in Alzheimer's disease.

A;Reference number: A49795; MUID:91273117; PMID:1905108

A;Accession: A49795

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-695 <POD>

A;Cross-references: GB:M58727; NID:g342062; PIDN:AAA36829.1; PID:g342063

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing

Query Match 99.5%; Score 3633; DB 1; Length 695;
 Best Local Similarity 99.7%; Pred. No. 1.5e-183;
 Matches 693; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI PYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI PYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF	600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695

RESULT 2

QRHUA4

Alzheimer's disease amyloid beta protein precursor [validated] - human

N;Alternate names: Alzheimer's disease amyloid A4 protein; coagulation factor XIa inhibitor; proteinase nexin II (PN-II)

N;Contains: amyloid beta protein long, plaque form; amyloid beta protein short, vascular form; amyloid protein precursor splice form APP(695); amyloid protein precursor splice form APP(751); amyloid protein precursor splice form APP(770)

C;Species: Homo sapiens (man)

C;Date: 30-Jun-1987 #sequence_revision 28-Jul-1995 #text_change 15-Sep-2000

C;Accession: S02260; S05194; A32277; A33260; A35486; I39452; I39451; I39453; I59562; A44017; B44017; A03134; A29030; A47584; A47585; S02638; S00707; S00925; A38949; A30320; B30320; C30320; A31087; A24668; A28583; A29302; A60805; JL0038; S06121; A60355; A59011; A38384; S29076; S38252; S32539; S48148; S48692; S51186; S51185; S51184; S51183; A54238; I58075; I52250; S09010; S10737; S24127; S43644

R;Lemaire, H.G.; Salbaum, J.M.; Multhaup, G.; Kang, J.; Bayney, R.M.; Unterbeck, A.; Beyreuther, K.; Mueller-Hill, B.

Nucleic Acids Res. 17, 517-522, 1989

A;Title: The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid is encoded by 16 exons.

A;Reference number: S02260; MUID:89128427; PMID:2783775

A;Accession: S02260

A;Molecule type: DNA

A;Residues: 1-288, 'V', 365-770 <LEM1>

A;Cross-references: EMBL:X13466

A;Note: alternative splice form APP(695)

R;Lemaire, H.G.

submitted to the EMBL Data Library, November 1988

A;Reference number: S05194

A;Accession: S05194

A;Molecule type: DNA

A;Residues: 1-14, 'VW', 17-288, 'V', 365-770 <LEM2>

A;Cross-references: EMBL:X13466; NID:g35598; PIDN:CAA31830.1; PID:g871360

A;Note: alternative splice form APP(695)

R;La Fauci, G.; Lahiri, D.K.; Salton, S.R.J.; Robakis, N.K.

Biochem. Biophys. Res. Commun. 159, 297-304, 1989

A;Title: Characterization of the 5'-end region and the first two exons of the beta-protein precursor gene.

A;Reference number: A32277; MUID:89165870; PMID:2538123

A;Accession: A32277

A;Molecule type: DNA

A;Residues: 1-75 <LAF>

A;Cross-references: GB:M24546; GB:M24547; NID:g341202; PIDN:AAC13654.1; PID:g516074

R;Johnstone, E.M.; Chaney, M.O.; Moore, R.E.; Ward, K.E.; Norris, F.H.; Little, S.P.

Biochem. Biophys. Res. Commun. 163, 1248-1255, 1989

A;Title: Alzheimer's disease amyloid peptide is encoded by two exons and shows similarity to soybean trypsin inhibitor.

A;Reference number: A33260; MUID:89392030; PMID:2675837

A;Accession: A33260

A;Molecule type: DNA

A;Residues: 656-737 <JOH>

A;Cross-references: GB:M29270; NID:gl78863; PIDN:AAA51768.1; PID:gl78865

R;Prelli, F.; Levy, E.; van Duinen, S.G.; Bots, G.T.A.M.; Luyendijk, W.; Frangione, B.

Biochem. Biophys. Res. Commun. 170, 301-307, 1990

A;Title: Expression of a normal and variant Alzheimer's beta-protein gene in amyloid of hereditary cerebral hemorrhage, Dutch type: DNA and protein diagnostic assays.

A;Reference number: A35486; MUID:90321244; PMID:2196878
 A;Accession: A35486
 A;Molecule type: DNA
 A;Residues: 672-710 <PRE1>
 A;Note: 693-Gln was found in DNA isolated from HCHWA-D patients
 R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.
 Gene 87, 257-263, 1990
 A;Title: Genomic organization of the human amyloid beta-protein precursor gene.
 A;Reference number: I39451; MUID:90236318; PMID:2110105
 A;Accession: I39452
 A;Status: nucleic acid sequence not shown; translation not shown; translated
 from GB/EMBL/DDBJ
 A;Molecule type: DNA
 A;Residues: 1-770 <YOS1>
 A;Cross-references: GB:M33112; NID:g178613; PIDN:AAB59502.1; PID:g178616
 A;Accession: I39451
 A;Status: nucleic acid sequence not shown; translation not shown; translated
 from GB/EMBL/DDBJ
 A;Molecule type: DNA
 A;Residues: 1-530, 'QWLMPVIPAFWEAKVGR' <YOS2>
 A;Cross-references: GB:M34875; NID:g178608; PIDN:AAB59501.1; PID:g178615
 R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.
 Gene 102, 291-292, 1991
 A;Reference number: A59020; MUID:91340168; PMID:1908403
 A;Contents: annotation; erratum
 A;Note: revised physical map for reference I39451
 R;Levy, E.; Carman, M.D.; Fernandez-Madrid, I.J.; Power, M.D.; Lieberburg, I.;
 van Duinen, S.G.; Bots, G.T.; Luyendijk, W.; Frangione, B.
 Science 248, 1124-1126, 1990
 A;Title: Mutation of the Alzheimer's disease amyloid gene in hereditary cerebral
 hemorrhage, Dutch type.
 A;Reference number: I39453; MUID:90260663; PMID:2111584
 A;Accession: I39453
 A;Status: translated from GB/EMBL/DDBJ
 A;Molecule type: DNA
 A;Residues: 656-737 <LEV>
 A;Cross-references: GB:M37896; NID:g178618; PIDN:AAA51727.1; PID:g178620
 A;Note: a mutation with 693-Gln is presented
 R;Murrell, J.; Farlow, M.; Ghetti, B.; Benson, M.D.
 Science 254, 97-99, 1991
 A;Title: A mutation in the amyloid precursor protein associated with hereditary
 Alzheimer's disease.
 A;Reference number: I59562; MUID:92022553; PMID:1925564
 A;Accession: I59562
 A;Status: translated from GB/EMBL/DDBJ
 A;Molecule type: DNA
 A;Residues: 689-716, 'F', 718-737 <MUR>
 A;Cross-references: GB:S57665; NID:g236720; PIDN:AAB19991.1; PID:g236721
 R;Kamino, K.; Orr, H.T.; Payami, H.; Wijsman, E.M.; Alonso, M.E.; Pulst, S.M.;
 Anderson, L.; O'dahl, S.; Nemens, E.; White, J.A.; Sadovnick, A.D.; Ball, M.J.;
 Kaye, J.; Warren, A.; McInnis, M.; Antonarakis, S.E.; Korenberg, J.R.; Sharma,
 V.; Kukull, W.; Larson, E.; Heston, L.L.; Martin, G.M.; Bird, T.D.;
 Schellenberg, G.D.
 Am. J. Hum. Genet. 51, 998-1014, 1992
 A;Title: Linkage and mutational analysis of familial Alzheimer disease kindreds
 for the APP gene region.
 A;Reference number: A44017; MUID:93035397; PMID:1415269

A;Accession: A44017
 A;Molecule type: DNA
 A;Residues: 687-692, 'G', 694-718 <KAM1>
 A;Cross-references: GB:S45135; NID:g257377; PIDN:AAB23645.1; PID:g257378
 A;Experimental source: familial Alzheimer disease family SB
 A;Note: sequence extracted from NCBI backbone (NCBIP:115374)
 A;Accession: B44017
 A;Molecule type: DNA
 A;Residues: 687-718 <KAM2>
 A;Cross-references: GB:S45136; NID:g257379; PIDN:AAB23646.1; PID:g257380
 A;Experimental source: familial Alzheimer disease family LIT
 A;Note: sequence extracted from NCBI backbone (NCBIP:115376)
 A;Note: this sequence has a silent mutation
 R;Kang, J.; Lemaire, H.G.; Unterbeck, A.; Salbaum, J.M.; Masters, C.L.;
 Grzeschik, K.H.; Multhaup, G.; Beyreuther, K.; Muller-Hill, B.
 Nature 325, 733-736, 1987
 A;Title: The precursor of Alzheimer's disease amyloid A4 protein resembles a
 cell-surface receptor.
 A;Reference number: A03134; MUID:87144572; PMID:2881207
 A;Accession: A03134
 A;Molecule type: mRNA
 A;Residues: 1-288, 'V', 365-770 <KAN>
 A;Cross-references: GB:Y00264; NID:g28525; PIDN:CAA68374.1; PID:g28526
 A;Note: alternative splice form APP(695)
 R;Robakis, N.K.; Ramakrishna, N.; Wolfe, G.; Wisniewski, H.M.
 Proc. Natl. Acad. Sci. U.S.A. 84, 4190-4194, 1987
 A;Title: Molecular cloning and characterization of a cDNA encoding the
 cerebrovascular and the neuritic plaque amyloid peptides.
 A;Reference number: A29030; MUID:87231971; PMID:3035574
 A;Accession: A29030
 A;Molecule type: mRNA
 A;Residues: 284-288, 'V', 365-646, 'E', 648-770 <ROB>
 A;Cross-references: GB:M16765; NID:g178539; PIDN:AAA51722.1; PID:g178540
 A;Note: the authors translated the codon GAG for residue 647 as Asp
 R;Goldgaber, D.; Lerman, M.I.; McBride, O.W.; Saffiotti, U.; Gajdusek, D.C.
 Science 235, 877-880, 1987
 A;Title: Characterization and chromosomal localization of a cDNA encoding brain
 amyloid of Alzheimer's disease.
 A;Reference number: A47584; MUID:87120328; PMID:3810169
 A;Accession: A47584
 A;Molecule type: mRNA
 A;Residues: 674-756, 'S', 758-770 <GOL>
 A;Cross-references: GB:M15533; NID:g178706; PIDN:AAA35540.1; PID:g178707
 A;Experimental source: brain
 R;Tanzi, R.E.; Gusella, J.F.; Watkins, P.C.; Bruns, G.A.P.; St George-Hyslop,
 P.; Van Keuren, M.L.; Patterson, D.; Pagan, S.; Kurnit, D.M.; Neve, R.L.
 Science 235, 880-884, 1987
 A;Title: Amyloid beta protein gene: cDNA, mRNA distribution, and genetic linkage
 near the Alzheimer locus.
 A;Reference number: A47585; MUID:87120329; PMID:2949367
 A;Accession: A47585
 A;Molecule type: mRNA
 A;Residues: 674-703 <TAN1>
 A;Cross-references: GB:M15532; NID:g177957; PIDN:AAA51564.1; PID:g177958
 R;Dyrks, T.; Weidemann, A.; Multhaup, G.; Salbaum, J.M.; Lemaire, H.G.; Kang,
 J.; Mueller-Hill, B.; Masters, C.L.; Beyreuther, K.
 EMBO J. 7, 949-957, 1988

A;Title: Identification, transmembrane orientation and biogenesis of the amyloid A4 precursor of Alzheimer's disease.
 A;Reference number: S02638; MUID:88296437; PMID:2900137
 A;Accession: S02638
 A;Molecule type: mRNA
 A;Residues: 672-678 <DYR>
 R;Tanzi, R.E.; McClatchey, A.I.; Lamperti, E.D.; Villa-Komaroff, L.; Gusella, J.F.; Neve, R.L.
 Nature 331, 528-530, 1988
 A;Title: Protease inhibitor domain encoded by an amyloid protein precursor mRNA associated with Alzheimer's disease.
 A;Reference number: S00707; MUID:88122640; PMID:2893290
 A;Accession: S00707
 A;Molecule type: mRNA
 A;Residues: 286-344,'I',365-366 <TAN2>
 A;Cross-references: EMBL:X06982; NID:g28817; PIDN:CAA30042.1; PID:g929612
 A;Experimental source: promyelocytic leukemia cell line HL60
 A;Note: alternative splice form APP(751)
 R;Ponte, P.; Gonzalez-DeWhitt, P.; Schilling, J.; Miller, J.; Hsu, D.; Greenberg, B.; Davis, K.; Wallace, W.; Lieberburg, I.; Fuller, F.; Cordell, B.
 Nature 331, 525-527, 1988
 A;Title: A new A4 amyloid mRNA contains a domain homologous to serine proteinase inhibitors.
 A;Reference number: S00925; MUID:88122639; PMID:2893289
 A;Accession: S00925
 A;Molecule type: mRNA
 A;Residues: 1-344,'I',365-770 <PO2>
 A;Cross-references: GB:X06989; EMBL:Y00297; NID:g28720; PIDN:CAA30050.1; PID:g28721
 A;Note: alternative splice form APP(751)
 R;Kitaguchi, N.; Takahashi, Y.; Tokushima, Y.; Shiojiri, S.; Ito, H.
 Nature 331, 530-532, 1988
 A;Title: Novel precursor of Alzheimer's disease amyloid protein shows protease inhibitory activity.
 A;Reference number: A38949; MUID:88122641; PMID:2893291
 A;Accession: A38949
 A;Molecule type: mRNA
 A;Residues: 287-367 <KIT>
 A;Cross-references: GB:X06981; NID:g28816; PIDN:CAA30041.1; PID:g929611
 A;Experimental source: glioblastoma cell line
 A;Note: alternative splice form APP(770)
 R;Vitek, M.P.; Rasool, C.G.; de Sauvage, F.; Vitek, S.M.; Bartus, R.T.; Beer, B.; Ashton, R.A.; Macq, A.F.; Maloteaux, J.M.; Blume, A.J.; Octave, J.N.
 Brain Res. Mol. Brain Res. 4, 121-131, 1988
 A;Title: Absence of mutation in the beta-amyloid cDNAs cloned from the brains of three patients with sporadic Alzheimer's disease.
 A;Reference number: A30320
 A;Accession: A30320
 A;Status: not compared with conceptual translation
 A;Molecule type: mRNA
 A;Residues: 284-288,'V',365-770 <VIT1>
 A;Accession: B30320
 A;Status: not compared with conceptual translation
 A;Molecule type: mRNA
 A;Residues: 122-288,'V',365-770 <VIT2>
 A;Accession: C30320
 A;Status: not compared with conceptual translation

A;Molecule type: mRNA

A;Residues: 606-770 <VIT3>

R;Zain, S.B.; Salim, M.; Chou, W.G.; Sajdel-Sulkowska, E.M.; Majocha, R.E.; Marotta, C.A.

Proc. Natl. Acad. Sci. U.S.A. 85, 929-933, 1988

A;Title: Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer disease brain: coding and noncoding regions of the fetal precursor mRNA are expressed in the cortex.

A;Reference number: A31087; MUID:88124954; PMID:2893379

A;Accession: A31087

A;Molecule type: mRNA

A;Residues: 507-770 <ZAI>

A;Cross-references: GB:M18734; NID:g178572; PIDN:AAA51726.1; PID:g178573

A;Note: the authors translated the codon GAA for residue 599 as Gly, ACC for residue 603 as Val, GTG for residue 604 as Glu, GAG for residue 605 as Leu, CTT for residue 607 as Pro, CCC for residue 608 as Val, GTG for residue 609 as Asn, AAT for residue 610 as Gly, and GGT for residue 655 as Ser

A;Note: the cited Genbank accession number, J03594, is not in release 101.0

R;Masters, C.L.; Multhaup, G.; Simms, G.; Pottgiesser, J.; Martins, R.N.; Beyreuther, K.

Query Match 98.1%; Score 3582.5; DB 1; Length 770;
Best Local Similarity 89.9%; Pred. No. 7.8e-181;
Matches 692; Conservative 2; Mismatches 1; Indels 75; Gaps 1;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
      |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVR----- 288
      |||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVREVCSEQAETGPC 300

Qy    289 ----- 288

Db    301 RAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSAMSQSLLKTTQEPLARD 360

Qy    289 ---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA 345
      :|||
Db    361 PVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA 420

Qy    346 KNLPKADKKAVIQHFQEKVESLEQEANERQQLVETHMARVEAMLNDRRRLALENYITAL 405
      |||
Db    421 KNLPKADKKAVIQHFQEKVESLEQEANERQQLVETHMARVEAMLNDRRRLALENYITAL 480
```

Qy 406 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 465
 |||
 Db 481 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 540
 |||
 Qy 466 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTET 525
 |||
 Db 541 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTET 600
 |||
 Qy 526 KTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN 585
 |||
 Db 601 KTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN 660
 |||
 Qy 586 IKTEEISEVNLDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 645
 ||| : |||
 Db 661 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 720
 |||
 Qy 646 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
 |||
 Db 721 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 770
 |||

RESULT 3

S00550

Alzheimer's disease amyloid beta protein precursor - rat

N;Alternate names: beta-A4 amyloid protein

C;Species: Rattus norvegicus (Norway rat)

C;Date: 30-Jun-1989 #sequence_revision 30-Jun-1989 #text_change 13-Aug-1999

C;Accession: S00550; A41245; A39820; S46251

R;Shivers, B.D.; Hilbich, C.; Multhaup, G.; Salbaum, M.; Beyreuther, K.;

Seeburg, P.H.

EMBO J. 7, 1365-1370, 1988

A;Title: Alzheimer's disease amyloidogenic glycoprotein: expression pattern in rat brain suggests a role in cell contact.

A;Reference number: S00550; MUID:88312583; PMID:2900758

A;Accession: S00550

A;Molecule type: mRNA

A;Residues: 1-695 <SHI>

A;Cross-references: EMBL:X07648; NID:g55616; PIDN:CAA30488.1; PID:g55617

R;Schubert, D.; Schroeder, R.; LaCorbiere, M.; Saitoh, T.; Cole, G.

Science 241, 223-226, 1988

A;Title: Amyloid beta protein precursor is possibly a heparan sulfate proteoglycan core protein.

A;Reference number: A41245; MUID:88264430; PMID:2968652

A;Accession: A41245

A;Molecule type: protein

A;Residues: 18-37, 'X', 39-40, 'X', 42-44 <SCH>

A;Note: evidence for heparan sulfate attachment

R;Hesse, L.; Beher, D.; Masters, C.L.; Multhaup, G.

FEBS Lett. 349, 109-116, 1994

A;Title: The beta-A4 amyloid precursor protein binding to copper.

A;Reference number: S46251; MUID:94320627; PMID:7913895

A;Contents: annotation; copper binding sites

A;Note: rat peptides were isolated but not sequenced

R;Potempska, A.; Styles, J.; Mehta, P.; Kim, K.S.; Miller, D.L.

J. Biol. Chem. 266, 8464-8469, 1991

A;Title: Purification and tissue level of the beta-amyloid peptide precursor of rat brain.

A;Reference number: A39820; MUID:91217087; PMID:1673681

A;Accession: A39820

A;Status: preliminary

A;Molecule type: protein

A;Residues: 18-32 <POT>

A;Experimental source: brain

C;Comment: Deposition of amyloid protein as neurofibrillary tangles and/or plaques is characteristic of both Alzheimer's disease and Down's syndrome.

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; amyloid; glycoprotein; transmembrane protein F;625-648/Domain: transmembrane #status predicted <TMM>

Query Match 96.9%; Score 3536; DB 2; Length 695;
Best Local Similarity 97.0%; Pred. No. 1.9e-178;
Matches 674; Conservative 8; Mismatches 13; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      ||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      1 MLPSLALLLLAAWTVRALEVPTDGNAGLLAEPQIAMFCGKLNMHMNVQNGKWESDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      ||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db     61 TCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHTHIVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    181 GVEFVCCPLAEESDSIDSADAEEDSDVWWGGADTDYADGGEDKVVEVAEEEEVADVEEE 240

Qy    241 EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
      ||: |||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    241 EAEDDEDVEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF 360
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPHVFNMLK 420
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
      ||||| || ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    541 DDLQPWHPFGVDSVPANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF 600
```



```

Qy      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660
      |||||:|||||
Db      601 GHDSGFVVRHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660

Qy      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
      |||||
Db      661 VEVDAAVTPEERHLSKMOONGYENPTYKFFEOMON 695

```


A;Title: A Xenopus homologue of the human beta-amyloid precursor protein: developmental regulation of its gene expression.
A;Reference number: JH0773; MUID:93129227; PMID:1282805
A;Accession: JH0773
A;Molecule type: mRNA
A;Residues: 1-747 <OKA>
A;Cross-references: GB:S52417; NID:g263150; PIDN:AAB24853.1; PID:g263151
A;Experimental source: larva
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; amyloid
F;287-337/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

Query Match 84.8%; Score 3095; DB 2; Length 747;
Best Local Similarity 80.8%; Pred. No. 3e-155;
Matches 596; Conservative 36; Mismatches 42; Indels 64; Gaps 5;

```

Qy      17 ALEVPTDGNAGLLAEPQIAMF-CGRLNMHMNVQNGKWSDPSGKTCTCIDTKEGILQYCQE 75
      |||| ||| ||||||||| |||||||||:| || || |||||||||
Db      15 ALEVLVDGNGGLLAEPQIAMFSVARLNMHMNVQNGKWETDVSG---CIGTKEGILQYCQE 71

Qy      76 VYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDALLVPDKCKF 135
      |||||||||||||||||||:|||||: | |:|||||||||||||||
Db      72 VYPELQITNVVEANQPVTIQNWCKKGRKQCKSRTHIVVPYRCLVGEFVSDALLVPDKCKF 131

Qy     136 LHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCCPLAEESDN 195
      |||||||:|||||:|||||:|:|:||||||||||| |||::
Db     132 LHQERMDICETHLHWHTVAKESCSEKSM SLHEYGMLLPCGIDKFRGVEFVCCPSAESESE 191

Qy     196 VDSADAEEDSDVWVGADTDYADGSEDKVVEVA--EEEEVAEVEEEEADDDDEDDEDGDE 253
      ||||| ||| ||||||| || | |:| || || |||| ||||| ||||
Db     192 FDSADAAEDDCDVWVGADADYVDRSDDKAVEAQPD EEEEVVEVEEEEETDDDED--DGDE 249

Qy     254 VEEEAEEPYEEATERTTSIATTTTTTTTSESVEEVVR----- 288
      ||| |||||||||||||||||||||||||
Db     250 AEEPEEPYEEATERTTSIATTTTTTTTSESVEEVVREVCSEQAETGPCRAMISRWYYDVTE 309

Qy     289 -----VPTTAASTPDAVDKYLETPGDENEHAHFQ 317
      :| |||||||||||| | |||| |
Db     310 SKCAQFIYGGCGGNRNNFESDDYCMVCGSVIPATAASTPDAVDKYLENPNDENEHDRFL 369

Qy     318 KAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEKVESLEQEAAANERQQ 377
      ||||| |||:|:|:|:|||||||||||||||||||||:|
Db     370 KAKERLEGKHREKMSEVMKEWEEAERQAKNLPKADKKAVIQHFQEKVESLEQEAAKQRQQ 429

Qy     378 LVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHF 437
      |||||||||||||||:||||||| |||||||||||||||||
Db     430 LVETHMARVEAMLNDRRRIALENYITALQADPPRPRHVFNMLKKYVRAEQKDRQHTLKHF 489

Qy     438 EHVRMVDPKKAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVAEEIQDEVDELLQKEQNY 497
      ||||||||||||||||| ||||| ||| ||||||||| |||||
Db     490 EHVRMVDPKKAQIRSQVMTHLRVINERMNQSFSLLYKVPVAVAEEIQDEVDEL FQKEQNY 549

Qy     498 SDDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFLDDLPWHSFGADSV PAN 557
      |||::|:|:| |:|:|||||||:|||||||:|:|:|:||||||| |||||
Db     550 SDDMVSNMVS DHRVSYGNDALMPSLSETKTTVELLPVDGEFNIEDLPWHSFGVDSVPAN 609

```

```

Qy      558 TENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEFRHDSGYEVHHQKLVFFA 617
          ||||||||||||||||||||||||||||||||||| :|||: ||| |||||||
Db      610 TENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDSEYRHDTAYEVHHQKLVFFA 669

Qy      618 EDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGVVEVDAAVTPEERHLSKM 677
          |:|||||||||||||||||||||||||||:|||||||||||||||:|
Db      670 EEVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTTIHGGVVEVDAAVTPEERHLTKM 729

Qy      678 QQNGYENPTYKFFEQMQN 695
          |||||||
Db      730 QQNGYENPTYKFFEQMQN 747

```

RESULT 6

A32761

hypothetical Alzheimer's disease amyloid beta protein, Alu-containing clone - human (fragment)

C;Species: Homo sapiens (man)

C;Date: 29-Jan-1990 #sequence_revision 10-Apr-1996 #text_change 10-Apr-1996

C;Accession: A32761

R;de Sauvage, F.; Octave, J.N.

Science 245, 651-653, 1989

A;Title: A novel mRNA of the A4 amyloid precursor gene coding for a possibly secreted protein.

A;Reference number: A32761; MUID:89346754; PMID:2569763

A;Accession: A32761

A;Molecule type: mRNA

A;Residues: 1-484 <DES>

A;Cross-references: GB:M28373

A;Note: the authors translated the codon ATG for residue 433 as Leu

C;Comment: This is the hypothetical translation of a sequence believed to contain cloning artifacts.

C;Keywords: cloning artifact

```

Query Match          57.7%;  Score 2105;  DB 4;  Length 484;
Best Local Similarity 87.7%;  Pred. No. 1.8e-103;
Matches 407;  Conservative 1;  Mismatches 0;  Indels 56;  Gaps 1;

```

```

Qy      80 LQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDALLVPDKCKFLHQE 139
          |||||||||||||||||||||||||||||||||||
Db      1  LQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDALLVPDKCKFLHQE 60

Qy     140 RMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCCPLAEESDNVDSA 199
          |||||||||||||||||||||||||||||||||||
Db      61 RMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCCPLAEESDNVDSA 120

Qy     200 DAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEEADDDDEDGDEVEEEAE 259
          |||||||||||||||||||||||||||||||||||
Db     121 DAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEEADDDDEDGDEVEEEAE 180

Qy     260 EPYEEATERTTSIATTTTTTTTESVEEVVR----- 288
          |||||||||||||||||||
Db     181 EPYEEATERTTSIATTTTTTTTESVEEVREVCSEQAETGPCRAMISRWFYDVTGKCAPF 240

Qy     289 -----VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERL 323
          :||||||||||||||
Db     241 FYGGCGGNRNNFDTEEYCMVCGSAIPTTAASTPDAVDKYLETPGDENEHAHFQKAKERL 300

```

Qy 324 EAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQEKVESLEQEAAANERQQLVETHM 383
 |||
 Db 301 EAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQEKVESLEQEAAANERQQLVETHM 360

Qy 384 ARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMV 443
 |||
 Db 361 ARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMV 420

Qy 444 DPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQDEV 487
 |||
 Db 421 DPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQDEV 464

RESULT 7

A49321

amyloid beta (A4) homolog 2 precursor - human

N;Alternate names: CDEI-binding protein

C;Species: Homo sapiens (man)

C;Date: 24-Feb-1994 #sequence_revision 18-Nov-1994 #text_change 13-Aug-1999

C;Accession: A49321; S34644; S40519

R;Sprecher, C.A.; Grant, F.J.; Grimm, G.; O'Hara, P.J.; Norris, F.; Norris, K.; Foster, D.C.

Biochemistry 32, 4481-4486, 1993

A;Title: Molecular cloning of the cDNA for a human amyloid precursor protein homolog: evidence for a multigene family.

A;Reference number: A49321; MUID:93250009; PMID:8485127

A;Accession: A49321

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-763 <SPR>

A;Cross-references: GB:S60099; NID:g300168; PIDN:AAC60589.1; PID:g300169

A;Experimental source: placenta

A;Note: sequence extracted from NCBI backbone (NCBIN:131198, NCBI:131199)

A;Note: expression was shown in placenta, brain, heart, lung, liver, and kidney

R;von der Kammer, H.; Klaudiny, J.; Hanes, J.; Scheit, K.H.

submitted to the EMBL Data Library, April 1993

A;Description: The human homologue of the murine CDEI binding protein is an amyloid precursor like protein.

A;Reference number: S34644

A;Accession: S34644

A;Molecule type: mRNA

A;Residues: 1-763 <VON>

A;Cross-references: EMBL:Z22572; NID:g394763; PIDN:CAA80295.1; PID:g394764

R;Wasco, W.; Gurubhagavatula, S.; Paradis, M.; Romano, D.M.; Sisodia, S.S.;

Hyman, B.T.; Neve, R.L.; Tanzi, R.E.

Nature Genet. 5, 95-99, 1993

A;Title: Isolation and characterization of APLP2 encoding a homologue of the Alzheimer's associated amyloid beta protein precursor.

A;Reference number: S40519; MUID:94035131; PMID:8220435

A;Accession: S40519

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-763 <WAS>

A;Cross-references: GB:L27631; NID:g450391; PIDN:AAC41701.1; PID:g450392

C;Genetics:

A;Gene: GDB:APLP2; APPL2

A;Cross-references: GDB:139159; OMIM:104776

A;Map position: 11q23-11q25

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing; transmembrane protein

F;310-360/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

Query Match 47.2%; Score 1725; DB 2; Length 763;
Best Local Similarity 46.9%; Pred. No. 2.9e-83;
Matches 369; Conservative 112; Mismatches 170; Indels 136; Gaps 19;

```
Qy      5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWDSDP 56
      | | | | | | | | | | : | | | | | | | | | | | | | | | | | | | | | |
Db     15 LLLLLLVGLTAPALALAGYIEALANAGTGFVAEAPQIAMFCGKLNMHVNIQTGKWEPPD 74

Qy     57 SGTKTCTIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
      : | | | : | | | : | | | | | | | | | | | | | | | | | | | | | | | |
Db     75 TGTKSCFETKEEVLQYCQEMYPELQITNVMEANQRVSIDNWCRRDKKQCKS--RFVTPFK 132

Qy    117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176
      | | | | | | | | | | : | | | : | | | | | | | | | | | | | | | | |
Db    133 CLVGEFVSDVLLVPEKQOFFHKERMEVCENHQHWHHTVVKEACLTQGMTLYSYGMLLPCGV 192

Qy    177 DKFRGVEFVCCPLAEESDNVDSADAEEDSDVWGGADTDYADGSEDKVVEVAEEEEVAE 236
      | : | | | | | | : : | : | | : : | | | | : | | | :
Db    193 DQFHGTEYVCCPQTKIIGSVSKEEEEEDEE-----EEEEDEEEDYDVYKSEFPTEAD 245

Qy    237 VEE--EEA--DDDEDDDEDGDEVEEEAEOPY-----EEATERTTSIATTTTTTTTES 282
      : | : | | : | | | : | | | | : : | | | | : : |
Db    246 LEDFTEAAVDEDEDEEEGEEVVEDRDYYYDTFKGDDYNEENPTEPGSDGTMSDKEITHD 305

Qy    283 VEEV-----VRVP 290
      | : | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    306 VKAVCSQEAMTGPCRAVMPRWYFDLSKGKCVRFIYGGCGGNRNFESEDYCMVCKAMIP 365

Qy    291 TTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPK 350
      | | | | | | | | | | : | | | | | | | | | | : | | | | | | | | | |
Db    366 PTPLPTND-VDVYFETSADDNEHARFQKAKEQLEIRHRNRMDRVKKWEAAELQAKNLPK 424

Qy    351 ADKKAVIQHFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPP 410
      | : : : | | | | | : | | | | : | | | | | | | | | | : | | | | |
Db    425 AERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRRMALENYLAALQSDPP 484

Qy    411 RPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSL 470
      | | : | : | | | | | | | | : | : | | | | | | | | | | | | | | |
Db    485 RPHRILQALRRYVRAENKDRDLHTIRHYQHVLAVDPEKAAQMKSQVMTHLHVIEERNQSL 544

Qy    471 SLLYNVPAVAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTVE 530
      | | | | | | | | : | | | : | | | | : : | | | | | | | | | |
Db    545 SLLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTASISETPVDVR 587

Qy    531 LLPVNGEFSDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPG-----SGLTN 585
      | : | | : : | : | | | | | | | | | | : | | | | | | | | | |
Db    588 ---VSSEES-EEIPPFHPPF--HPFPALPENE---DTQPELYHPMKKSGVGEQDGGGLIG 637

Qy    586 IKTEEISEVN-LDAEFRHDSGYEVHHQKLVFFAEDVGS-----NKGAI 627
      : : | : | : | | : | : : : | | | | | | | | | | : | :
```

Db 638 AEEKVINSKNKVDENMVIDETLDV--KEMIFNAERVGGLEERESVGPLREDFSLSSAL 695

Qy 628 IGLMVGGVVIATVIVITLVMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTY 687
 |||:| | |||||:||||:|:| | ||:|||| :|||||:||| :|||||

Db 696 IGLLVIAVAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQNHHGYENPTY 755

Qy 688 KFFEQQMQ 694
 |: ||||

Db 756 KYLEQQMQ 762

RESULT 8

S42880

amyloid precursor-like protein - rat

C;Species: Rattus norvegicus (Norway rat)

C;Date: 06-Jan-1995 #sequence_revision 06-Jan-1995 #text_change 17-Mar-1999

C;Accession: S42880; S47528

R;Sandbrink, R.; Masters, C.L.; Beyreuther, K.

submitted to the EMBL Data Library, March 1994

A;Description: Complete nucleotide and deduced amino acid sequence of rat amyloid precursor-like protein 2 (Aplp2/Apph): Two amino acids length difference to human and murine homologues.

A;Reference number: S42880

A;Accession: S42880

A;Molecule type: mRNA

A;Residues: 1-765 <SAN>

A;Cross-references: EMBL:X77934

R;Sandbrink, R.; Masters, C.L.; Beyreuther, K.

Biochim. Biophys. Acta 1219, 167-170, 1994

A;Title: Complete nucleotide and deduced amino acid sequence of rat amyloid protein precursor-like protein 2 (APLP2/APPH): two amino acids length difference to human and murine homologues.

A;Reference number: S47528; MUID:94368849; PMID:8086458

A;Accession: S47528

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-765 <SA2>

A;Cross-references: EMBL:X77934

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

C;Keywords: alternative splicing

F;312-362/Domain: animal Kunitz-type proteinase inhibitor homology <BPI>

Query Match . 46.8%; Score 1709; DB 2; Length 765;

Best Local Similarity 45.9%; Pred. No. 2e-82;

Matches 361; Conservative 124; Mismatches 168; Indels 134; Gaps 20;

Qy 5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWDS DP 56
 | :||| || | : ||| :|||||||:||||:|:| |||: ||

Db 15 LLVLLLLGLTAPAAALAGYIEALAANAGTGFAVAEPQIAMFCGKLNMHVNIQTGKWE PD 74

Qy 57 SGTKTCTIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
 :|||:|: ||| :|||||:|||||||:||||| | :||:| :|||:| | |||:|

Db 75 TGTKSCLGTKEEVLQYCQEIYPELQITNVMEANQPVNIDSWCRRDKKQCRS--HIVIPFK 132

Qy 117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176
 |||||||| ||||: |:| |||||:||| | |||| || | : |: |||||||:

Db 133 CLVGEFVSDVLLVPENCQFFHQERMEVCEKHQRWHTVVKEACLTEGMTLYSYGMLLPCGV 192
 Qy 177 DKFRGVEFVCCPLAE--ESDNVDSADAEEDSDVWVGADTDYA-DGSEDKVVEVAEEEE 233
 | : | | : | | | : : | | : | : | : : : | | | | | :
 Db 193 DQFHGTEYVCCPQTKVVDSDSTMSKEEEEEEE---DEEDYALDKSEFPTEADLEDFT 248
 Qy 234 VAEVEEEEADDDDEDEDGDEVEEEAEOPYEE-----ATERTTSIATTTTTTTTESVEEV 287
 | : | : | : : | : | : | : | : | : | : | : | : | : | : | :
 Db 249 EAAADEDEDEEEEEEEEGEEVVEDRDYYYDSFKGDDYNEENPTEPSSDGTISDKIEAHDV 308
 Qy 288 R-----VPT 291
 : :
 Db 309 KAVCSQEAMTGPCRAVMRWYFDLSKGKCVRFIYGGCGNRNNFESEDYCMVCKTMIPP 368
 Qy 292 TAASTPDAVDKYLETPGDENEHAFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKA 351
 | | | | | | : | | | | | | : | | | | : | | | | | | | | | |
 Db 369 TPLPTND-VDVYFETSADDNEHARFQKAKEQLEIRHRSRMDRVKKEWEEAELQAKNLPKA 427
 Qy 352 DKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPR 411
 : : : | | | | : : | : | : | : | : | : | : | : | : | : | : | :
 Db 428 ERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRRIALENYLAALQSDPPR 487
 Qy 412 PRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLS 471
 | : | : | | | | | | | : : | : | | : | | | : | | | | | | | | | |
 Db 488 PHRILQALRRYVRAENKDRLHTIRHYQHVLAVDPEKAAQMKSQVMTHLHVIEERRNQSLS 547
 Qy 472 LLYNVPAAVEEIQDEVDLQKEQNYSDDLANMISEPRISYGNLALMPSLTETKTTVEL 531
 | | | | | : | : | : | : | : | : : : : : | : | : | : |
 Db 548 LLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTSSISENPVDVR- 589
 Qy 532 LPVNGEFLDDLQPWHSFGADSVPAANTENEVEPVDARP-----AADRGLTTRPGSGLTN 585
 | : | | : : | : | | : : | : | : | : | : | : | : | : | : | :
 Db 590 --VSSEES-EEIPPFHPF--HPFPSSLSENE----DTQPELYHPMKKSGSGMAEQDG-GLIG 639
 Qy 586 IKTEEISEVN-LDAEFRHDSGYEVHHQKLVFFAEDVGS-----NKGAI 627
 : : | : | : | : | : | : : : | | | : :
 Db 640 AEEKVINSKNKMDENMVIDETLDV--KEMIFNAERVGGLEEEPD SVGPLREDFSLSSAL 697
 Qy 628 IGLMVGGVVIATVIVITLVMLKKKQYTSIHGGVVEVDAAVTPEERHL SKMQONGYENPTY 687
 | | : | | | | | : | | : | : | : | : | : | : | : | : | : | : | : | : | :
 Db 698 IGLLVIAVAIATVIVISLVMLRKRQYGTISHGIVEVHPMLTPEERHLNKMQN HGYENPTY 757
 Qy 688 KFFEQQMQ 694
 | : | | |
 Db 758 KYLEQQMQ 764

RESULT 9

A49974

beta-amyloid precursor protein 2 homolog APLP2 - mouse

C;Species: Mus musculus (house mouse)

C;Date: 06-Oct-1994 #sequence_revision 18-Nov-1994 #text_change 13-Aug-1999

C;Accession: A49974

R;Slunt, H.H.; Thinakaran, G.; Von Koch, C.; Lo, A.C.; Tanzi, R.E.; Sisodia, S.S.

J. Biol. Chem. 269, 2637-2644, 1994


```

Qy      522 LTETKTTVELLPVNGEFLDDLPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGS 581
      :| | : | : | | | | : :| | | | : : |
Db      579 ISENPVDVRVSSESE-EIPPFHPLHPF-----PSLSENE-----GSGMAEQDG- 621

Qy      582 GLTNIKTEEISEVN-LDAEFRHDSGYEVHHQKLVFFAEDVGS-----N 623
      || : : | : | : | : | : : : | | | | :
Db      622 GLIGAEKVINSKNKMMDENMVIDETLDV--KEMIFNAERVGGLEEEPESVGPLREDFSL 679

Qy      624 KGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGVEVDAAVTPEERHLSKMQQNGYE 683
      | : | | : | | | | | | : | | : | | | : | | | | : | | | : | |
Db      680 SNALIGLLVIAVAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQNHYGE 739

Qy      684 NPTYKFFEQMQ 694
      | | | | : | | |
Db      740 NPTYKYLEQMQ 750

```

RESULT 10

A46362

amyloid precursor-like protein - mouse

C;Species: Mus musculus (house mouse)

C;Date: 21-Sep-1993 #sequence_revision 18-Nov-1994 #text_change 24-Nov-1999

C;Accession: A46362

R;Wasco, W.; Bupp, K.; Magendantz, M.; Gusella, J.F.; Tanzi, R.E.; Solomon, F.
Proc. Natl. Acad. Sci. U.S.A. 89, 10758-10762, 1992

A;Title: Identification of a mouse brain cDNA that encodes a protein related to
the Alzheimer disease-associated amyloid beta protein precursor.

A;Reference number: A46362; MUID:93066322; PMID:1279693

A;Accession: A46362

A;Status: preliminary

A;Molecule type: nucleic acid

A;Residues: 1-653 <WAS>

A;Experimental source: brain

A;Note: sequence inconsistent with the nucleotide translation

A;Note: sequence extracted from NCBI backbone (NCBIN:118683, NCBIP:118684)

C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
proteinase inhibitor homology

C;Keywords: transmembrane protein

Query Match 32.4%; Score 1183; DB 2; Length 653;

Best Local Similarity 39.0%; Pred. No. 7.1e-55;

Matches 275; Conservative 121; Mismatches 221; Indels 88; Gaps 20;

```

Qy      1 MLPGLALLLLAAWTARA-LEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGT 59
      :| | :| | | | | | | : | | | | :| :| | | :| :| :| | :
Db      22 LLP-LSLLLLRAQLAVGNLAVGSPSAAEAPGSAQVAGLCGRLTLHRDLRTGRWEPDPQRS 80

Qy      60 KTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHF-VIPYRCL 118
      : | : : :| :| :| | | | | | | : | :| :| :| | | | | :| :| :|
Db      81 RRCLLDLPQRVLEYCRQMPYELHIARVEQAAQAI PMERWCGGTRSGRCAHPHHEVVPFHCL 140

Qy      119 VGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDK 178
      | | | | :| | | | :| :| | | | | | | | : | :| | | : | | | | | :|
Db      141 PGEFVSEALLVPEGCRFLHQERMDQCESSTRRHQEAQAEACSSQGLILHGSGMLLPCGSDR 200

Qy      179 FRGVEFVCCPLAEESDNVDSADAEEDDSVDVW-WGGADTDYADGSEDKVVEVAEEEEVAEV 237
      | | | | :| | | : | :| :| :| :| :| :| :| :| :| :|

```

```

Db      201 FRGVEYVCCP-PPATPNPSGMAAGDPSTRSWPLGGR----AEGGED-----EEEVESF 248
Qy      238 EEEEADDDDEDDGDEVEEEAEEPVEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTP 297
      : | : :| || | : | : : | | ||
Db      249 PQPVDDYFVEPPQAEAAAAAAAAEERAPPPSSHTPVMVSRVTPTPR-----PT----- 294
Qy      298 DAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVI 357
      | | | | : || : || : || : : || || : | : || || || : :
Db      295 DGVDVYFGMPGEIGEHEGFLRAKMDLEERRMRQINEVMREWAMADSQSKNLPKADRQALN 354
Qy      358 QHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFN 417
      : || | : : || : : | || : || | | : : || | | : | |
Db      355 EHFQSILQTLQVSGERQRLVETHATRVIALINDQRRAALEGFLAALQGDPPQAERVLM 414
Qy      418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP 477
      | : : || || | : : || | || : || | : || | || || || |
Db      415 ALRRYLRAEQKEQRHTLRHYQHVAVDPEKAQQMRQVQVQTHLQVIEERMNQSLSGLLDQNP 474
Qy      478 AVAEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMP-SLTETKTTVELLPVNG 536
      : || : : || | | : : | : | : |
Db      475 HLAQELRPQIQELL-----LAEHLGPSEL---DASVPGSSSEDK----- 510
Qy      537 EFSLDDLQPWHSFGADSVPAANTENEVEPVDPARPAADRGLTTRPGSG-----LTNIKTEEI 591
      || | | : : | | : | | : | | : |
Db      511 ----GSLQP-----PESKDDPPVTLP---KGSTDQESSSSGREKLTPLEQYE- 550
Qy      592 SEVNLDAEFRHDSGYEVHH---QKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVML 648
      : || | : | : | : : | : | : : | : : : :
Db      551 QKVNASA----PRGFPHSSDIQRDELAPSGTGVSREALSGLLIMAGGGSLIVLSLLLL 606
Qy      649 -KKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQ 692
      || | : | || || | : || : | : : || || || : |
Db      607 RKKKPYGTISHGVVEVDPMLTLEEQQQLRELQRHGYENPTYRFLEE 651

```

RESULT 11

JC1404

CDEI-box DNA-binding protein - mouse

C;Species: Mus musculus (house mouse)

C;Date: 30-Sep-1993 #sequence_revision 30-Sep-1993 #text_change 16-Feb-1997

C;Accession: JC1404

R;Vidal, F.; Blangy, A.; Rassoulzadegan, M.; Cuzin, F.

Biochem. Biophys. Res. Commun. 189, 1336-1341, 1992

A;Title: A murine sequence-specific DNA binding protein shows extensive local similarities to the amyloid precursor protein.

A;Reference number: JC1404; MUID:93129193; PMID:1482349

A;Accession: JC1404

A;Molecule type: mRNA

A;Residues: 1-511 <VID>

C;Comment: This protein plays an important role in the early development of the mouse.

C;Keywords: DNA binding; transmembrane protein

Query Match 31.2%; Score 1138; DB 2; Length 511;

Best Local Similarity 45.4%; Pred. No. 1.2e-52;

Matches 251; Conservative 93; Mismatches 129; Indels 80; Gaps 16;

A;Experimental source: strain Bristol N2; clone C42D8
R;Daigle, I.; Li, C.
Proc. Natl. Acad. Sci. U.S.A. 90, 12045-12049, 1993
A;Title: *apl-1*, a *Caenorhabditis elegans* gene encoding a protein related to the human beta-amyloid protein precursor.
A;Reference number: A49414; MUID:94089766; PMID:8265668
A;Accession: A49414
A;Status: preliminary
A;Molecule type: mRNA
A;Residues: 7-686 <DAI>
A;Cross-references: GB:U00240; NID:g416296; PIDN:AAC46470.1; PID:g416297
C;Genetics:
A;Gene: CESP:C42D8.8
A;Map position: X
A;Introns: 22/3; 78/3; 121/1; 199/1; 230/1; 274/3; 344/3; 410/2; 471/2; 537/3; 580/3
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

```

Db      415 RINGTLAMLRDFPDLEKYVRPIAVTYWKDYRDEVSPDISVE----DSELTPIIHDDEFSK 470
Qy      514 GN--DALMPSLT----ETKTTVELLPVNGEFLDDLQPWHSFGADSVPAANT---ENEVEP 564
      |  | : |  :  : : |  | : :  |  | : : |
Db      471 NAKLDVKAPTTTAKPVKETDNAKVLPTASDSEEEADEYYEDEDDEQVKKTPDMKKKKVKV 530
Qy      565 VДАРP-----AADRGLTTRPGSGLTNIKTEE-----ISEVNLDA 598
      || : |  |  |  |  |  | : : : |  | : : |
Db      531 VDIKPKEIKVTIEEEKKAPKLVETSVQTDEDDDEDESSSSTSSESEDEDEDKNIKELRVDI 590
Qy      599 E-----FRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLK 649
      |  : ||  || : |  |  |  | : :  | | |  :
Db      591 EPIIDEPASFYRHD-----KLIQSPEVERSASSVFQPYVLASAMFITAICIIFAIT 642
Qy      650 KKQYTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFE 691
      :  | : ||  || || : : || || || || || || :
Db      643 NARRRRAMRGFIEVD-VYTPEERHVAGMQVNGYENPTYSFDD 683

```

RESULT 13

A32758

beta-amyloid-like protein precursor - fruit fly (*Drosophila melanogaster*)

C;Species: *Drosophila melanogaster*

C;Date: 08-Dec-1989 #sequence_revision 08-Dec-1989 #text_change 24-Sep-1998

C;Accession: A32758

R;Rosen, D.R.; Martin-Morris, L.; Luo, L.; White, K.

Proc. Natl. Acad. Sci. U.S.A. 86, 2478-2482, 1989

A;Title: A *Drosophila* gene encoding a protein resembling the human beta-amyloid protein precursor.

A;Reference number: A32758; MUID:89184650; PMID:2494667

A;Accession: A32758

A;Status: preliminary

A;Molecule type: mRNA

A;Residues: 1-886 <ROS>

A;Cross-references: GB:J04516; NID:g158371; PID:g158372

C;Genetics:

A;Gene: FlyBase:Appl

A;Cross-references: FlyBase:FBgn0000108

C;Keywords: transmembrane protein

Query Match 20.4%; Score 746; DB 2; Length 886;

Best Local Similarity 25.5%; Pred. No. 9.4e-32;

Matches 233; Conservative 126; Mismatches 289; Indels 264; Gaps 29;

```

Qy      7 LLLLAAWTARALEVPTDGNAGLLA-----EPQIAMFC--GRLNMHMNV-QNGKWDSDPG 58
      ||| : |  | :  | | : |  |||| : |  | : :  : : | : | |
Db      9 LLLRSLWVVLAI-----GTAQVQAASPRWEPQIAVLCEAGQIQPYLSEGRWVTDLSK 63
Qy      59 T---KTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRG---RKQCKTHPHFV 112
      || : |  : | || : : ||  || : || : :  |  || : |  : ||  : :
Db      64 KTTGPTCLRDKMDLLDYCKKAYPNRDITNIVESSHYQKIGGWCRQGALNAAKCKGSHRWI 123
Qy      113 IPYRCLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLL 172
      | : || | | | || || : | | |  |  : :  |  | :  : : || |
Db      124 KPFRCL-GPFQSDALLVPEGCLFDHIHNASRCWPFVRWNQTGAAACQERGMQMRTFAMLL 182
Qy      173 PCGIDKFRGVEFVCCP-----LAESDNVD---SA 199

```

```

      |||| | |||||
Db      183 PCGISVFSGVFVCCPKHFKTDEIHVKKTDLVMPAAQINSANDELMNDEDDSDNSNYSK 242
Qy      200 DAEEDDSVWVGADTDYADGSEDKVVEVAEEEEV-----AEV 237
      || ||| | | | :| :| ||
Db      243 DANEDDL-----DEDDLMDGDEEDDMVADEAATAGGSPNTGSSGDSNSGSLDDINA EY 296
Qy      238 EE-EEADDDDEDGDEVEEEAE EPY-----EEATERT 269
      : || | :| | | | | : | :| :
Db      297 DSGEEDNYEEDGAGSESEAEVEASWDQSGGAKVVSLSKSDSSSPSSAPVAPAPEKAPVKS 356
Qy      270 TSIATTTTTTTSVEEV-----RVPTTAASTPDAVDKYLETPGDENEHAHFQK 318
      | : :| : : | | :| | | | | || :
Db      357 ESVTSTPQLSASAAAFVAANSNGSGTGAGAPPSTAQPTS---DPYFTHFDPHYEHQSYKV 413
Qy      319 AKERLEAKHRERMSQVMREWEAEERQAKNLPKADKKA-----VIQHFQEKVESLEQEA 371
      : :||| ||| : :| :| : :| || : || | :| :|
Db      414 SQKRLEESHREKVTRVMKDWSDLEEKYQDMRLADPKAAQSFQRM TARFQTSVQALEEEG 473
Qy      372 ANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQ 431
      | : || | || | :| | :| | | || || | :| :| ||
Db      474 NAEKHQLAAMHQQRVLAHINQRKREAMTCYTQALTEQPPNAHHVEKCLQKLLRALHKDRA 533
Qy      432 HTLKHFEH-VRMVDP---KKAQIIRSQVMTHLRVIYERMNQSLSLLYNVPAVAEEI---- 483
      | | | : | : | : || | : : | | : ||| :| | : :|
Db      534 HALAHYRHLNLSGGPGGLEAAASERPRTLRLIDIDRAVNQSMTMLKRYPELSAKIAQLM 593
Qy      484 -----QDEV----- 487
      :| :
Db      594 NDYILALRSKDDIPGSSSLGMSEAEAGILDKYRVEIERKVAEKERLRLAEKQKQRAAE 653
Qy      488 -----DELLQKEQNYSDDLANMISE-----PRISYGNDALM 519
      :| | : | || : :| | | | :
Db      654 REKLREEKLRLAEKKVDDMLKSQVAEQQSQPTQSSTQSQAQQQQQEKSLPGKELGPDAA 713
Qy      520 -----PSLTETKTTVELLPVNGEFSLLDLPWHSFGADSV PANTENEVEPV DARPAADRG 574
      | :| || : | | | : :| :| | | | |
Db      714 VTAANPNLETTKS-----EKDLSDE---YGEATVSTTKVQTVLPTVDDDAVQRA 760
Qy      575 LTTRPGSGLTNIKTEEISEVNLDAEFRHDSGYEVHHQKLVF-----FAEDVGSNK---GA 626
      : : : : :| : :| :| :| :|
Db      761 VEDVAAA-----VAHQEAEPQVQHFMTHDLGHRESSFSRLRREFAQHAHA AKEGRNV 811
Qy      627 IIGLMVGGVVIATVIVITLVMLKKKQYTSIH-HGVVEVDAAVTP-----EERHLSKMQQ 679
      | | : : : : | : | | :|| | | | :| : ||
Db      812 YFTLSFAGIALMAAVFVGVA VAKWRTSRSPHAQGFIEVDQNVTTTHPIVREEKIVPNMQI 871
Qy      680 NGYENPTYKFFE 691
      ||||| :|
Db      872 NGYENPTYKYFE 883

```

RESULT 14

S38344

CDEI-binding protein - mouse (fragment)

C;Species: Mus musculus (house mouse)

C;Date: 19-May-1994 #sequence_revision 26-May-1995 #text_change 03-May-1996

C;Accession: S38344
 R;Hanes, J.; von der Kammer, H.; Kristjansson, G.I.; Scheit, K.H.
 Biochim. Biophys. Acta 1216, 154-156, 1993
 A;Title: The complete cDNA coding sequence for the mouse CDEI binding protein.
 A;Reference number: S38344; MUID:94032480; PMID:8218408
 A;Accession: S38344
 A;Status: preliminary
 A;Molecule type: mRNA
 A;Residues: 1-246 <HAN>
 A;Cross-references: EMBL:Z22592
 C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type
 proteinase inhibitor homology

Query Match 19.3%; Score 706; DB 2; Length 246;
 Best Local Similarity 51.5%; Pred. No. 2.4e-30;
 Matches 136; Conservative 35; Mismatches 51; Indels 42; Gaps 7;

```

Qy      5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWSDSP 56
      | :|||  || | :          |||  :||| ||| ||:||||:| ||: ||
Db      15 LLVLLLGLTAPAAALAGYIEALAANAGTGFAVAEPQIAMLCGKLNMHVNIQTGKWEPPD 74

Qy     57 SGTKTCTIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
      :|||:|: ||| :||| |||:||||| ||| ||| | :||:| :|||: | |||:
Db     75 TGTKSCLGTKEEVLQYCQEIYPELQITNVMEANQPVNIDSWCRRDKRQCKS--HIVIPFK 132

Qy    117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176
      ||||| ||| ||| :| |||: ||| | |||: || | : | : |||||:
Db    133 CLVGEFVSDVLLVPDNCQFFHQERMEVCEKHQRWHTLVKEACLTEGLTLYSYGMLLPCGV 192

Qy    177 DKFRGVEFVCCPLAEESDNVDSADAEEDSDVWGGADTDYADGSEDKVVEVAEEEEVAE 236
      |:| | |:|||  :: |||          | : |||
Db    193 DQFHGTEYVCCP---QTKTVDS-----DSTMSKEEEEE--- 222

Qy    237 VEEEEEADDED-DEDGDEVEEEAE 259
      ||:| |:||| | | | ||:
Db    223 -EEDEEEDDYDLDKSEFPTEAD 245
  
```

RESULT 15

PQ0438

Alzheimer's disease amyloid A4 protein precursor - rabbit (fragment)

C;Species: Oryctolagus cuniculus (domestic rabbit)

C;Date: 30-Sep-1993 #sequence_revision 19-Oct-1995 #text_change 19-Oct-1995

C;Accession: PQ0438; C60045

R;Davidson, J.S.; West, R.L.; Kotikalapudi, P.; Maroun, L.E.

Biochem. Biophys. Res. Commun. 188, 905-911, 1992

A;Title: Sequence and methylation in the beta/A4 region of the rabbit amyloid precursor protein gene.

A;Reference number: PQ0438; MUID:93075180; PMID:1445331

A;Accession: PQ0438

A;Molecule type: DNA

A;Residues: 1-82 <DAV>

A;Cross-references: GB:M83558; GB:M83657

R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.

Brain Res. Mol. Brain Res. 10, 299-305, 1991

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:46:43 ; Search time 44.3333 Seconds
 (without alignments)
 4923.349 Million cell updates/sec

Title: US-09-806-194A-18
 Perfect score: 3651
 Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62
 Gapop 10.0 , Gapext 0.5

Searched: 1288442 seqs, 313154207 residues

Total number of hits satisfying chosen parameters: 1288442

Minimum DB seq length: 0
 Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
 Maximum Match 100%
 Listing first 45 summaries

Database : Published Applications_AA:*

- 1: /cgn2_6/ptodata/1/pubpaa/US07_PUBCOMB.pep:*
- 2: /cgn2_6/ptodata/1/pubpaa/PCT_NEW_PUB.pep:*
- 3: /cgn2_6/ptodata/1/pubpaa/US06_NEW_PUB.pep:*
- 4: /cgn2_6/ptodata/1/pubpaa/US06_PUBCOMB.pep:*
- 5: /cgn2_6/ptodata/1/pubpaa/US07_NEW_PUB.pep:*
- 6: /cgn2_6/ptodata/1/pubpaa/PCTUS_PUBCOMB.pep:*
- 7: /cgn2_6/ptodata/1/pubpaa/US08_NEW_PUB.pep:*
- 8: /cgn2_6/ptodata/1/pubpaa/US08_PUBCOMB.pep:*
- 9: /cgn2_6/ptodata/1/pubpaa/US09A_PUBCOMB.pep:*
- 10: /cgn2_6/ptodata/1/pubpaa/US09B_PUBCOMB.pep:*
- 11: /cgn2_6/ptodata/1/pubpaa/US09C_PUBCOMB.pep:*
- 12: /cgn2_6/ptodata/1/pubpaa/US09_NEW_PUB.pep:*
- 13: /cgn2_6/ptodata/1/pubpaa/US10A_PUBCOMB.pep:*
- 14: /cgn2_6/ptodata/1/pubpaa/US10B_PUBCOMB.pep:*
- 15: /cgn2_6/ptodata/1/pubpaa/US10C_PUBCOMB.pep:*
- 16: /cgn2_6/ptodata/1/pubpaa/US10_NEW_PUB.pep:*
- 17: /cgn2_6/ptodata/1/pubpaa/US60_NEW_PUB.pep:*
- 18: /cgn2_6/ptodata/1/pubpaa/US60_PUBCOMB.pep:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result	Score	Query	Match	Length	ID	Description
No.						

1	3651	100.0	697	9	US-09-794-927-18	Sequence 18, Appl
2	3651	100.0	697	9	US-09-795-847-18	Sequence 18, Appl
3	3651	100.0	697	9	US-09-794-743-18	Sequence 18, Appl
4	3651	100.0	697	9	US-09-794-748-18	Sequence 18, Appl
5	3651	100.0	697	9	US-09-794-925-18	Sequence 18, Appl
6	3651	100.0	697	9	US-09-681-442-18	Sequence 18, Appl
7	3651	100.0	697	10	US-09-869-414-18	Sequence 18, Appl
8	3651	100.0	697	10	US-09-548-366-18	Sequence 18, Appl
9	3651	100.0	697	12	US-10-652-927-18	Sequence 18, Appl
10	3651	100.0	697	12	US-10-652-830-18	Sequence 18, Appl
11	3643	99.8	697	9	US-09-794-927-16	Sequence 16, Appl
12	3643	99.8	697	9	US-09-795-847-16	Sequence 16, Appl
13	3643	99.8	697	9	US-09-794-743-16	Sequence 16, Appl
14	3643	99.8	697	9	US-09-794-748-16	Sequence 16, Appl
15	3643	99.8	697	9	US-09-794-925-16	Sequence 16, Appl
16	3643	99.8	697	9	US-09-681-442-16	Sequence 16, Appl
17	3643	99.8	697	10	US-09-869-414-16	Sequence 16, Appl
18	3643	99.8	697	10	US-09-548-366-16	Sequence 16, Appl
19	3643	99.8	697	12	US-10-652-927-16	Sequence 16, Appl
20	3643	99.8	697	12	US-10-652-830-16	Sequence 16, Appl
21	3641	99.7	695	9	US-09-794-927-12	Sequence 12, Appl
22	3641	99.7	695	9	US-09-795-847-12	Sequence 12, Appl
23	3641	99.7	695	9	US-09-794-743-12	Sequence 12, Appl
24	3641	99.7	695	9	US-09-794-748-12	Sequence 12, Appl
25	3641	99.7	695	9	US-09-794-925-12	Sequence 12, Appl
26	3641	99.7	695	9	US-09-681-442-12	Sequence 12, Appl
27	3641	99.7	695	10	US-09-869-414-12	Sequence 12, Appl
28	3641	99.7	695	10	US-09-548-366-12	Sequence 12, Appl
29	3641	99.7	695	12	US-10-652-927-12	Sequence 12, Appl
30	3641	99.7	695	12	US-10-652-830-12	Sequence 12, Appl
31	3641	99.7	695	15	US-10-427-208-46	Sequence 46, Appl
32	3638	99.6	697	9	US-09-794-927-20	Sequence 20, Appl
33	3638	99.6	697	9	US-09-795-847-20	Sequence 20, Appl
34	3638	99.6	697	9	US-09-794-743-20	Sequence 20, Appl
35	3638	99.6	697	9	US-09-794-748-20	Sequence 20, Appl
36	3638	99.6	697	9	US-09-794-925-20	Sequence 20, Appl
37	3638	99.6	697	9	US-09-681-442-20	Sequence 20, Appl
38	3638	99.6	697	10	US-09-869-414-20	Sequence 20, Appl
39	3638	99.6	697	10	US-09-548-366-20	Sequence 20, Appl
40	3638	99.6	697	12	US-10-652-927-20	Sequence 20, Appl
41	3638	99.6	697	12	US-10-652-830-20	Sequence 20, Appl
42	3637	99.6	695	15	US-10-427-208-25	Sequence 25, Appl
43	3637	99.6	695	15	US-10-427-208-27	Sequence 27, Appl
44	3637	99.6	695	15	US-10-427-208-28	Sequence 28, Appl
45	3636	99.6	695	15	US-10-427-208-31	Sequence 31, Appl

ALIGNMENTS

RESULT 1

US-09-794-927-18

; Sequence 18, Application US/09794927

; Patent No. US20010016324A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

```

; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280FG
; CURRENT APPLICATION NUMBER: US/09/794,927
; CURRENT FILING DATE: 2001-02-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 18
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-794-927-18

```

```

Query Match          100.0%; Score 3651; DB 9; Length 697;
Best Local Similarity 100.0%; Pred. No. 1.1e-223;
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

```

Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDADF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDADF	600
Qy	601	RHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIVITLMLKKKQYTSIHGGV	660
Db	601	RHDSGYEVHHQKLFFFAEDVGSNKGAIIGLMVGGVVIATVIVITLMLKKKQYTSIHGGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 2

US-09-795-847-18

; Sequence 18, Application US/09795847

; Patent No. US20010018208A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280DE

; CURRENT APPLICATION NUMBER: US/09/795,847

; CURRENT FILING DATE: 2001-02-28

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 18

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens
US-09-795-847-18

Query Match 100.0%; Score 3651; DB 9; Length 697;
Best Local Similarity 100.0%; Pred. No. 1.1e-223;
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVPYELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVPYELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540
        |||
Db    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
        |||
Db    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600

Qy    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITL VMLKKKQYTSIHHGV 660
        |||
Db    601 RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITL VMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
        |||
Db    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
```

RESULT 3

US-09-794-743-18
; Sequence 18, Application US/09794743
; Patent No. US20010021391A1
; GENERAL INFORMATION:
; APPLICANT: Gurney, Mark E.
; APPLICANT: Bienkowski, Michael J.
; APPLICANT: Heinrikson, Robert L.
; APPLICANT: Parodi, Luis A.
; APPLICANT: Yan, Riqiang
; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND
; TITLE OF INVENTION: USES
; TITLE OF INVENTION: THEREFOR
; FILE REFERENCE: 28341/6280BC
; CURRENT APPLICATION NUMBER: US/09/794,743
; CURRENT FILING DATE: 2001-02-27
; PRIOR APPLICATION NUMBER: 09/416,901
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 18
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-794-743-18

Query Match 100.0%; Score 3651; DB 9; Length 697;
Best Local Similarity 100.0%; Pred. No. 1.1e-223;
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300

Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
 |||
 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
 |||
 Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480
 |||
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
 |||
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
 |||
 Db 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
 |||
 Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQM QNKK 697
 |||
 Db 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQM QNKK 697

RESULT 4

US-09-794-748-18

; Sequence 18, Application US/09794748

; Patent No. US20020037315A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
 AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280JL

; CURRENT APPLICATION NUMBER: US/09/794,748

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 18
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-794-748-18

Query Match 100.0%; Score 3651; DB 9; Length 697;
Best Local Similarity 100.0%; Pred. No. 1.1e-223;
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDDEGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540
        |||
Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
        |||
Db    541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVM LKKKQYTSIHHGV 660
        |||
Db    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVM LKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697
```

Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697

RESULT 5

US-09-794-925-18

; Sequence 18, Application US/09794925

; Patent No. US20020064819A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280HI

; CURRENT APPLICATION NUMBER: US/09/794,925

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 18

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-794-925-18

Query Match 100.0%; Score 3651; DB 9; Length 697;

Best Local Similarity 100.0%; Pred. No. 1.1e-223;

Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
|
Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy 61 TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
|
Db 61 TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
|
Db 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
|
Db 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy 241 EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
 |||
 Db 241 EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAEERQAKNLPKADKKAVIQHF 360
 |||
 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAEERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
 |||
 Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480
 |||
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540
 |||
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
 |||
 Db 541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600

Qy 601 RHD SGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITL VMLKKKQYTSIHHGV 660
 |||
 Db 601 RHD SGYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITL VMLKKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697
 |||
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK 697

RESULT 6

US-09-681-442-18

; Sequence 18, Application US/09681442

; Patent No. US20020081634A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280FG

; CURRENT APPLICATION NUMBER: US/09/681,442

; CURRENT FILING DATE: 2001-04-05

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 18
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-681-442-18

Query Match 100.0%; Score 3651; DB 9; Length 697;
Best Local Similarity 100.0%; Pred. No. 1.1e-223;
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVI	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Qy	601	RHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660

Qy	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Db	541	DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK	697

RESULT 8

US-09-548-366-18

; Sequence 18, Application US/09548366

; Publication No. US20030104365A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND

; TITLE OF INVENTION: USES THEREFOR

; FILE REFERENCE: 28341/6280A

; CURRENT APPLICATION NUMBER: US/09/548,366

; CURRENT FILING DATE: 2000-04-12

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 65
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 18
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-548-366-18

Query Match 100.0%; Score 3651; DB 10; Length 697;
Best Local Similarity 100.0%; Pred. No. 1.1e-223;
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
        |||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
        |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
        |||
Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDADF 600
        |||
Db    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDADF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMKKKQYTSIHHGV 660
        |||
Db    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697
```

Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

RESULT 9

US-10-652-927-18

; Sequence 18, Application US/10652927

; Publication No. US20040043408A1

; GENERAL INFORMATION:

; APPLICANT: Gurney et al.

; TITLE OF INVENTION: Alzheimer's Disease Secretase, APP Substrates Therefor and Uses

; TITLE OF INVENTION: Therefor

; FILE REFERENCE: 29915/6280N3

; CURRENT APPLICATION NUMBER: US/10/652,927

; CURRENT FILING DATE: 2003-08-29

; PRIOR APPLICATION NUMBER: 09/794,925

; PRIOR FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 74

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 18

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-10-652-927-18

Query Match 100.0%; Score 3651; DB 12; Length 697;

Best Local Similarity 100.0%; Pred. No. 1.1e-223;

Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
|
Db 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
|
Db 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120

Qy 121 EFVSDALLVPDKCKFLHQRMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
|
Db 121 EFVSDALLVPDKCKFLHQRMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
|
Db 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

Qy 241 EADDDDEDDGDEVEEEAEEPVEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Db	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Db	541	DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697

RESULT 10

US-10-652-830-18

; Sequence 18, Application US/10652830

; Publication No. US20040048303A1

; GENERAL INFORMATION:

; APPLICANT: Gurney et al.

; TITLE OF INVENTION: Alzheimer's Disease Secretase, APP Substrates Therefor and Uses

; TITLE OF INVENTION: Therefor

; FILE REFERENCE: 29915/6280N1

; CURRENT APPLICATION NUMBER: US/10/652,830

; CURRENT FILING DATE: 2003-08-29

; PRIOR APPLICATION NUMBER: 09/794,925

; PRIOR FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 74

; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 18
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-10-652-830-18

Query Match 100.0%; Score 3651; DB 12; Length 697;
Best Local Similarity 100.0%; Pred. No. 1.1e-223;
Matches 697; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      |||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAAEPYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
      |||
Db    241 EADDDDEDDEDGDEVEEEAAEPYEEATERTTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360
      |||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
      |||
Db    361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
      |||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
      |||
Db    481 EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAAF 600
      |||
Db    541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAAF 600

Qy    601 RHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
      |||
Db    601 RHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy    661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
      |||
```

Db 661 VEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQNKK 697

RESULT 11

US-09-794-927-16

; Sequence 16, Application US/09794927

; Patent No. US20010016324A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280FG

; CURRENT APPLICATION NUMBER: US/09/794,927

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 16

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-794-927-16

Query Match 99.8%; Score 3643; DB 9; Length 697;

Best Local Similarity 99.7%; Pred. No. 3.4e-223;

Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
        |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
        |||
Db     61 TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        |||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
        |||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
```

Qy 241 EADDDDEDDGDEVEEEAEOPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
 |||
 Db 241 EADDDDEDDGDEVEEEAEOPYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAEERQAKNLPKADKKAVIQHF 360
 |||
 Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAEERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
 |||
 Db 361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
 |||
 Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFS 540
 |||
 Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFS 540

Qy 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNDAEF 600
 ||| :|||
 Db 541 DDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
 |||
 Db 601 RHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
 |||
 Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

RESULT 12

US-09-795-847-16

; Sequence 16, Application US/09795847

; Patent No. US20010018208A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
 AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280DE

; CURRENT APPLICATION NUMBER: US/09/795,847

; CURRENT FILING DATE: 2001-02-28

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 16
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-795-847-16

Query Match 99.8%; Score 3643; DB 9; Length 697;
Best Local Similarity 99.7%; Pred. No. 3.4e-223;
Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

```
Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHNMNVQNGKWDSDPSGTK 60
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHNMNVQNGKWDSDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240

Qy    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    241 EADDDDEDDEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHF 360

Qy    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPABA 480

Qy    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL 540
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEFSL 540

Qy    541 DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNLDAAF 600
        ||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    541 DDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAAF 600

Qy    601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
```

```

Db          601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 660
Qy          661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
Db          661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

```

RESULT 13

US-09-794-743-16

; Sequence 16, Application US/09794743

; Patent No. US20010021391A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280BC

; CURRENT APPLICATION NUMBER: US/09/794,743

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 16

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-794-743-16

Query Match 99.8%; Score 3643; DB 9; Length 697;

Best Local Similarity 99.7%; Pred. No. 3.4e-223;

Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

```

Qy          1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHNMNVQNGKWSDPSGK 60
Db          1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHNMNVQNGKWSDPSGK 60
Qy          61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVPIPYRCLVG 120
Db          61 TCIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVPIPYRCLVG 120
Qy          121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

```

Db 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240
 |||

Db 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE 240

Qy 241 EADDDDEDGDEVEEEAEEPYYEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300
 |||

Db 241 EADDDDEDGDEVEEEAEEPYYEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV 300

Qy 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF 360
 |||

Db 301 DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHF 360

Qy 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420
 |||

Db 361 QEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK 420

Qy 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480
 |||

Db 421 KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA 480

Qy 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540
 |||

Db 481 EEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL 540

Qy 541 DDLQPWHSFGADSVPAANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNDAEF 600
 ||| :|||

Db 541 DDLQPWHSFGADSVPAANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEF 600

Qy 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLMLKKKQYTSIHGGV 660
 |||

Db 601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLMLKKKQYTSIHGGV 660

Qy 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697
 |||

Db 661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMKNKK 697

RESULT 14

US-09-794-748-16

; Sequence 16, Application US/09794748

; Patent No. US20020037315A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR,
 AND

; TITLE OF INVENTION: USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280JL

; CURRENT APPLICATION NUMBER: US/09/794,748

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

```
; PRIOR FILING DATE: 1999-10-13
; PRIOR APPLICATION NUMBER: 60/155,493
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 09/404,133
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: PCT/US99/20881
; PRIOR FILING DATE: 1999-09-23
; PRIOR APPLICATION NUMBER: 60/101,594
; PRIOR FILING DATE: 1998-09-24
; NUMBER OF SEQ ID NOS: 73
; SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 16
; LENGTH: 697
; TYPE: PRT
; ORGANISM: Homo sapiens
US-09-794-748-16
```

Query Match 99.8%; Score 3643; DB 9; Length 697;
Best Local Similarity 99.7%; Pred. No. 3.4e-223;
Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDDGDEVEEEAAEPYEEATERTTSIATTTTTTTTESVVEEVRVPTTAASTPDAV	300
Db	241	EADDDDEDDGDEVEEEAAEPYEEATERTTSIATTTTTTTTESVVEEVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVA	480
Qy	481	EEIQDEVDELLOKEQNYSDDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLOKEQNYSDDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSL	540


```

Qy      541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF 600
          |||
Db      541 DDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF 600

Qy      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660
          |||
Db      601 RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV 660

Qy      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697
          |||
Db      661 VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQNKK 697

```

RESULT 15

US-09-794-925-16

; Sequence 16, Application US/09794925

; Patent No. US20020064819A1

; GENERAL INFORMATION:

; APPLICANT: Gurney, Mark E.

; APPLICANT: Bienkowski, Michael J.

; APPLICANT: Heinrikson, Robert L.

; APPLICANT: Parodi, Luis A.

; APPLICANT: Yan, Riqiang

; TITLE OF INVENTION: ALZHEIMER'S DISEASE SECRETASE, APP SUBSTRATES THEREFOR, AND USES

; TITLE OF INVENTION: THEREFOR

; FILE REFERENCE: 28341/6280HI

; CURRENT APPLICATION NUMBER: US/09/794,925

; CURRENT FILING DATE: 2001-02-27

; PRIOR APPLICATION NUMBER: 09/416,901

; PRIOR FILING DATE: 1999-10-13

; PRIOR APPLICATION NUMBER: 60/155,493

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 09/404,133

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: PCT/US99/20881

; PRIOR FILING DATE: 1999-09-23

; PRIOR APPLICATION NUMBER: 60/101,594

; PRIOR FILING DATE: 1998-09-24

; NUMBER OF SEQ ID NOS: 73

; SOFTWARE: PatentIn Ver. 2.0

; SEQ ID NO 16

; LENGTH: 697

; TYPE: PRT

; ORGANISM: Homo sapiens

US-09-794-925-16

Query Match 99.8%; Score 3643; DB 9; Length 697;

Best Local Similarity 99.7%; Pred. No. 3.4e-223;

Matches 695; Conservative 1; Mismatches 1; Indels 0; Gaps 0;

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60
          |||
Db      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60

Qy      61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
          |||

```

Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Db	241	EADDDDEDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPDAV	300
Qy	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Db	301	DKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHF	360
Qy	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Db	361	QEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLK	420
Qy	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Db	421	KYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNPAVA	480
Qy	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Db	481	EEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSL	540
Qy	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD AEF	600
		:	
Db	541	DDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMD AEF	600
Qy	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Db	601	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHHGV	660
Qy	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697
Db	661	VEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM QNKK	697

Search completed: July 26, 2004, 13:00:43
 Job time : 45.3333 secs

GenCore version 5.1.6
Copyright (c) 1993 - 2004 Compugen Ltd.

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:39:53 ; Search time 35.3333 Seconds
(without alignments)
6224.043 Million cell updates/sec

Title: US-09-806-194A-18
Perfect score: 3651
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 1017041 seqs, 315518202 residues

Total number of hits satisfying chosen parameters: 1017041

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : SPTREMBL_25:*
1: sp_archaea:*
2: sp_bacteria:*
3: sp_fungi:*
4: sp_human:*
5: sp_invertebrate:*
6: sp_mammal:*
7: sp_mhc:*
8: sp_organelle:*
9: sp_phage:*
10: sp_plant:*
11: sp_rodent:*
12: sp_virus:*
13: sp Vertebrate:*
14: sp_unclassified:*
15: sp_rvirus:*
16: sp_bacteriap:*
17: sp_cheap:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result	Query					
No.	Score	Match	Length	DB	ID	Description

1	3420	93.7	695	13	Q9DGJ8	Q9dgj8 gallus gall
2	3379	92.5	751	13	Q9DGJ7	Q9dgj7 gallus gall
3	3206	87.8	693	13	Q98SG0	Q98sg0 xenopus lae
4	3182	87.2	695	13	Q98SF9	Q98sf9 xenopus lae
5	3180	87.1	695	13	Q7ZXQ0	Q7zxq0 xenopus lae
6	3095	84.8	747	13	Q91963	Q91963 xenopus. ap
7	2956.5	81.0	699	13	Q57394	Q57394 narke japon
8	2759.5	75.6	569	13	Q9PVL1	Q9pvl1 gallus gall
9	2605	71.4	534	13	Q93296	Q93296 gallus gall
10	2562	70.2	678	13	Q7ZZT1	Q7zzt1 brachydanio
11	2524	69.1	738	13	Q90W28	Q90w28 brachydanio
12	2487.5	68.1	694	13	Q8UUR9	Q8uur9 brachydanio
13	2334	63.9	612	13	Q9I9E7	Q9i9e7 brachydanio
14	1920	52.6	384	11	Q8BPC7	Q8bpc7 mus musculu
15	1762	48.3	695	4	Q13861	Q13861 homo sapien
16	1746.5	47.8	669	4	Q14662	Q14662 homo sapien
17	1737	47.6	707	11	Q80US7	Q80us7 mus musculu
18	1735	47.5	695	11	Q64348	Q64348 mus musculu
19	1726	47.3	715	11	Q7TT34	Q7tt34 mus musculu
20	1701	46.6	763	11	Q61482	Q61482 mus musculu
21	1699	46.5	751	11	Q60709	Q60709 mus musculu
22	1650	45.2	472	13	Q8UUS0	Q8uus0 brachydanio
23	1345.5	36.9	357	13	Q8UUI8	Q8uui8 brachydanio
24	1301.5	35.6	522	4	Q9BT36	Q9bt36 homo sapien
25	1082	29.6	218	11	Q8BPV5	Q8bpv5 mus musculu
26	1048.5	28.7	523	4	Q14594	Q14594 homo sapien
27	794	21.7	357	13	Q7ZZT2	Q7zzt2 brachydanio
28	771	21.1	239	13	Q8UUI7	Q8uui7 brachydanio
29	569	15.6	113	13	Q8JH58	Q8jh58 chelydra se
30	561	15.4	182	11	Q9CYS4	Q9cys4 mus musculu
31	478	13.1	97	6	Q28673	Q28673 oryctolagus
32	435.5	11.9	140	13	Q800X9	Q800x9 chelydra se
33	385.5	10.6	82	4	Q16019	Q16019 homo sapien
34	381.5	10.4	82	4	Q16014	Q16014 homo sapien
35	379.5	10.4	82	4	Q16020	Q16020 homo sapien
36	368	10.1	79	11	Q35463	Q35463 cricetulus
37	358.5	9.8	160	11	Q9QZ78	Q9qz78 cavia sp. p
38	328	9.0	208	11	Q8R0R7	Q8r0r7 mus musculu
39	239	6.5	49	6	Q97917	Q97917 bos taurus
40	196.5	5.4	727	5	Q95TG7	Q95tg7 drosophila
41	196.5	5.4	5303	5	Q9V628	Q9v628 drosophila
42	194	5.3	785	5	Q9GQ82	Q9gq82 drosophila
43	192.5	5.3	556	5	Q95S93	Q95s93 drosophila
44	192.5	5.3	1110	13	Q91255	Q91255 petromyzon
45	191.5	5.2	556	5	Q9V7I9	Q9v7i9 drosophila

ALIGNMENTS

RESULT 1

Q9DGJ8

ID Q9DGJ8 PRELIMINARY; PRT; 695 AA.
AC Q9DGJ8;
DT 01-MAR-2001 (TrEMBLrel. 16, Created)
DT 01-MAR-2001 (TrEMBLrel. 16, Last sequence update)
DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)

DE Beta-amyloid precursor protein 695 isoform.
OS Gallus gallus (Chicken).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC Gallus.
OX NCBI_TaxID=9031;
RN [1]
RP SEQUENCE FROM N.A.
RA Sarasa M., Rodolosse A., Sorribas V.;
RT "Cloning of full-length chicken beta-amyloid precursor protein
RT isoforms.";
RL Submitted (JUL-2000) to the EMBL/GenBank/DDBJ databases.
DR EMBL; AF289218; AAG00593.1; -.
DR HSSP; P05067; 1BA4.
DR GO; GO:0016020; C:membrane; IEA.
DR InterPro; IPR008155; A4_APP.
DR InterPro; IPR008154; A4_extra.
DR InterPro; IPR001255; Beta-APP.
DR Pfam; PF02177; A4_EXTRA; 1.
DR Pfam; PF03494; Beta-APP; 1.
DR PRINTS; PR00203; AMYLOIDA4.
DR SMART; SM00006; A4_EXTRA; 1.
DR PROSITE; PS00319; A4_EXTRA; 1.
DR PROSITE; PS00320; A4_INTRA; 1.
SQ SEQUENCE 695 AA; 78565 MW; F201ED02AEC86D95 CRC64;

Query Match 93.7%; Score 3420; DB 13; Length 695;
Best Local Similarity 93.7%; Pred. No. 3e-197;
Matches 653; Conservative 18; Mismatches 22; Indels 4; Gaps 3;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGK	60
Db	1	MLPHLALLLLAAGAARALEVPADGNAGLLAEPQIAMFCGRLNMHMNVQNGKWESDPSGK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGWKQCNHGHPIVVPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKLLHQERMDVCETHLHWHTVAKESCSEKSMNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSDVWVGADTDYADGSEDKVVE--VAEEEEVAEVE	238
Db	181	GVEFVCCPLAEESDNLDSADAEDDDSDVWVGADADYADGSDDKVVEEQPEEDEELTVVE	240
Qy	239	EEEADDDDEDDGDEVEEEAEPEYEATERTTSIATTTTTTTESVEEVVRVPTTAASTPD	298
		: : : :	
Db	241	DEDADDD-DDDDGDEI-EETEEYEEATERTTSIATTTTTTTESVEEVVRVPTTAASTPD	298
Qy	299	AVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQ	358
Db	299	AVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQ	358
Qy	359	HFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNM	418
Db	359	HFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRIAENYITALQTVPPRPRHVFNM	418

Qy 419 LKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP 478
 |||
 Db 419 LKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSFLYNVP 478

Qy 479 VAEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVNGEF 538
 |||
 Db 479 VAEIQDEVDELLQKEQNYSDVLNMISEPRISYGN DALMPSLTETKTTVELLPVDGEF 538

Qy 539 SLDDLQPWHSFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD 598
 |||
 Db 539 SLDDLQPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNVKTEEVEVKMD 598

Qy 599 EFRHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVM LKKKQYTSIHH 658
 |||
 Db 599 EFRHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVM LKKKQYTSIHH 658

Qy 659 GVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
 |||
 Db 659 GVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695

RESULT 2

Q9DGJ7

ID Q9DGJ7 PRELIMINARY; PRT; 751 AA.
 AC Q9DGJ7;
 DT 01-MAR-2001 (TrEMBLrel. 16, Created)
 DT 01-MAR-2001 (TrEMBLrel. 16, Last sequence update)
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
 DE Beta-amyloid precursor protein 751 isoform.
 OS Gallus gallus (Chicken).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
 OC Gallus.
 OX NCBI_TaxID=9031;
 RN [1]
 RP SEQUENCE FROM N.A.
 RA Sarasa M., Rodolosse A., Sorribas V.;
 RT "Cloning of full-length chicken beta-amyloid precursor protein
 RT isoforms."
 RL Submitted (JUL-2000) to the EMBL/GenBank/DDBJ databases.
 DR EMBL; AF289219; AAG00594.1; -.
 DR HSSP; P05067; 1BA4.
 DR GO; GO:0016020; C:membrane; IEA.
 DR GO; GO:0004867; F:serine protease inhibitor activity; IEA.
 DR InterPro; IPR008155; A4_APP.
 DR InterPro; IPR008154; A4_extra.
 DR InterPro; IPR001255; Beta-APP.
 DR InterPro; IPR002223; Kunitz_BPTI.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR Pfam; PF03494; Beta-APP; 1.
 DR Pfam; PF00014; Kunitz_BPTI; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR PRINTS; PR00759; BASICPTASE.
 DR ProDom; PD000222; Kunitz_BPTI; 1.
 DR SMART; SM00006; A4_EXTRA; 1.
 DR SMART; SM00131; KU; 1.

Db 659 DSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMKKKQYTSIHHGVVE 718

Qy 663 VDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
 |||

Db 719 VDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 751

RESULT 3

Q98SG0

ID Q98SG0 PRELIMINARY; PRT; 693 AA.
 AC Q98SG0;
 DT 01-JUN-2001 (TrEMBLrel. 17, Created)
 DT 01-JUN-2001 (TrEMBLrel. 17, Last sequence update)
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
 DE Beta-amyloid precursor protein A.
 GN APP.
 OS Xenopus laevis (African clawed frog).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Amphibia; Batrachia; Anura; Mesobatrachia; Pipoidae; Pipidae;
 OC Xenopodinae; Xenopus.
 OX NCBI_TaxID=8355;
 RN [1]
 RP SEQUENCE FROM N.A.
 RA Van den Hurk W.H.;
 RL Thesis (2001), Department of Biological Sciences,
 RL University of Nijmegen, Nijmegen, Netherlands.
 DR EMBL; AJ298150; CAC37193.1; -.
 DR HSSP; P05067; 1HZ3.
 DR GO; GO:0016020; C:membrane; IEA.
 DR InterPro; IPR008155; A4_APP.
 DR InterPro; IPR008154; A4_extra.
 DR InterPro; IPR001255; Beta-APP.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR Pfam; PF03494; Beta-APP; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR SMART; SM00006; A4_EXTRA; 1.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 KW Signal.
 FT SIGNAL 1 18 POTENTIAL.
 SQ SEQUENCE 693 AA; 78568 MW; CAF1DF655C1AB653 CRC64;

Query Match 87.8%; Score 3206; DB 13; Length 693;
 Best Local Similarity 87.5%; Pred. No. 2.2e-184;
 Matches 610; Conservative 37; Mismatches 44; Indels 6; Gaps 4;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGTK 60
 ||| : ||:| | |||| ||| ||||| :||| :|||

Db 1 MLPHITLLVLTV-GALALEVPADGNGGLLAEPQIAMFCGKLNMHMNVQNGKWETDVS GTK 59

Qy 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG 120
 || ||||| :||| :| :|||

Db 60 GCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKKGRKQCKSRTHIVVPIYRCLVG 119

Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
 ||||| :||| :||| :|||

Db 120 EFVSDALLVPDKCKFLHQERMDICETHLHWHTVAKESCSEKSMLEHYGMLLPCGIDKFR 179

Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVA--EEEEVAEVE	238
Db	180	GVEFVCCPSAAEESFSFDSADA-EDDSDAWGGADADYVDRSDDKAVEAQPDDEEEVVEVE	238
Qy	239	EEEADDDDEDDGDGEVEEEAAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTPD	298
Db	239	EEETDDDED--DGDEAAEEPEEPEYEEATERTTSIATTTTTTTTESVEEVVRVPATAASTPD	296
Qy	299	AVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQ	358
Db	297	AVDKYLENPNDENEHDFLKAKEERLEGKHREKMSVEMKEWEEAERQAKNLPKADKKAVIQ	356
Qy	359	HFQEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFNM	418
Db	357	HFQEKVESLEQEAAANERQQVLVETHMARVEAMLNDRRRIALENYITALQADPPRPRHVFNM	416
Qy	419	LKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPA	478
Db	417	LKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYKVPA	476
Qy	479	VAEEIQDEVDDELLQKEQNYSDDLANMISEPRISYGNDAIMPSTLTETKTTVELLPVNGEF	538
Db	477	VAEEIQDEVDDELQKEQNYSDDMVSNMVSDFRVSYGNDAIMPSTLSETKTTVELLPVDGEF	536
Qy	539	SLDDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDA	598
Db	537	NIEDLQPWHSFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDS	596
Qy	599	EFRHDSGYEVHHQKLVFFAEVDGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHH	658
Db	597	EYRHDTAYEVHHQKLVFFAEVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTTIHH	656
Qy	659	GVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN	695
Db	657	GVVEVDAAVTPEERHLTKMOONGYENPTYKFFEOMON	693

DR EMBL; AJ298151; CAC37194.1; -.
DR HSSP; P05067; 1HZ3.
DR GO; GO:0016020; C:membrane; IEA.
DR InterPro; IPR008155; A4_APP.
DR InterPro; IPR008154; A4_extra.
DR InterPro; IPR001255; Beta-APP.
DR Pfam; PF02177; A4_EXTRA; 1.
DR Pfam; PF03494; Beta-APP; 1.
DR PRINTS; PR00203; AMYLOIDA4.
DR SMART; SM00006; A4_EXTRA; 1.
DR PROSITE; PS00319; A4_EXTRA; 1.
DR PROSITE; PS00320; A4_INTRA; 1.
KW Signal.
FT SIGNAL 1 18 POTENTIAL.
SQ SEQUENCE 695 AA; 78803 MW; DC14EB02AFB0204A CRC64;

Query Match 87.2%; Score 3182; DB 13; Length 695;
Best Local Similarity 87.0%; Pred. No. 6e-183;
Matches 607; Conservative 40; Mismatches 45; Indels 6; Gaps 5;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
||| : ||:| | | |||| ||| ||||| |||||:||||| |||||:| ||||
Db 1 MLPHITLLVLTA-GALALEVPADGNGGLLAEPQIAMFCGKLNMHMNVQNGKWETDVSGTK 59

Qy 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
|| ||||| ||||| ||||| |||||:||||| |||||:| |||||
Db 60 GCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKKGRKQCKSRTHIVVPYRCLVG 119

Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
||||| |||||:||||| |||||:|||| :||:||||| |||||
Db 120 EFVSDALLVPDKCKFLHQERMDICETHLHWHTVAKESCSEKIMSLHEYGMLLPCGIDKFR 179

Qy 181 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEV--AEVEEVAEVE 238
|||||| ||||:| |||| ||||| ||||| || | |:| || ||||| |||
Db 180 GVEFVCCPTAEESSESFDSADA-EDSDVWVGADADYVDRSDDKAVEAQPEEEEEVEVE 238

Qy 239 EEEADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVR-VPTTAASTP 297
|||||| |:| |||| ||| ||||| ||||| ||||| ||||| || || |||
Db 239 EEEADDD-DEDDGDETEEEPEPEYEEATERTTSIATTTTTTTESVEEVVRVPATAVSTP 297

Qy 298 DAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAEERQAKNLPKADKKAVI 357
|||||| | |||| | ||||| ||||:||||:||||:||||| ||||| |||||
Db 298 DAVDKYLENPNDENEHDFLKAKEKLEKHKREKMSVMEKEWEEAEERQAKNLPKADKKAVI 357

Qy 358 QHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFN 417
||||| ||||| ||||| |||||:||||| ||||| ||||| |||||
Db 358 QHFQEKVESLEQEAANERQQLVETHMARVEATLNDRRRRIALENYITALQADPPRPRHVFN 417

Qy 418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP 477
||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||
Db 418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYKVP 477

Qy 478 AVAAEQDEVDLLQKEQNYSDDLANMISEPRISYGNDAALMPSLTETKTTVELLPVNGE 537
||||| ||||| |||||:||||:||||:| |:| |||||:||||| |||||:|
Db 478 AVAAEQDEVDLQKEQNYSDDMVSNMVSDFRVSYGNDAALMPSLSETKTTVELLPVDGE 537

Qy 538 FSLDDLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLD 597


```

Db      120 EFVSDALLVPDKCKFLHQERMDICETHLHWHTVAKESCSEKIMSLHEYGMLLPCGIDKFR 179
Qy      181 GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEV--AEEEEVAEVE 238
        |||||: ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      180 GVEFVCCPTAEESFSDSADA-EDSDVWWGGADADYVDRSDDKAVEAQPEEEEEVVEVE 238
Qy      239 EEEADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTSEVEEVVR-VPTTAASP 297
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      239 EEEADDD-DDDDGDETEEEPEEPYEEATERTTSIATTTTTTTTSEVEEVVRVPATAVSTP 297
Qy      298 DAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVI 357
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      298 DAVDKYLENPNDENEHDFLKAERLEGGHREKMSQVMREWEAAERQAKNLPKADKKAVI 357
Qy      358 QHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFN 417
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      358 QHFQEKVESLEQEAAKERQQLVETHMARVEATLNDRRLALENYITALQADPPRPRHVFN 417
Qy      418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP 477
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYKVP 477
Qy      478 AVAEIIQDEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGE 537
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      478 AVAEIIQDEVDELQKEQNYSDMVSNMVSDFRVSYGNDAIMPSTETKTTVELLPVDGE 537
Qy      538 FSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNL 597
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      538 FNVEDLQPWHSFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNIKREEISEVKMD 597
Qy      598 AEFRHDSGYEVHHQKLVFFAEVGSNGKAIIGLMVGGVVIATVIVITLVMLKKKQYTSIH 657
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      598 SEYRHDAAYEVHHQKLVFFAEVGSNGKAIIGLMVGGVVIATVIVITLVMLKKKQYTTIH 657
Qy      658 HGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
        ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      658 HGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695

```

RESULT 6

Q91963

```

ID   Q91963      PRELIMINARY;      PRT;      747 AA.
AC   Q91963;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE   APP747.
GN   APP747.
OS   Xenopus.
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Amphibia; Batrachia; Anura; Mesobatrachia; Pipoidae; Pipidae;
OC   Xenopodinae.
OX   NCBI_TaxID=8353;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=93129227; PubMed=1282805;

```

RA Okado H., Okamoto H.;
 RT "A Xenopus homologue of the human beta-amyloid precursor protein:
 RT developmental regulation of its gene expression.";
 RL Biochem. Biophys. Res. Commun. 189:1561-1568(1992).
 DR EMBL; S52417; AAB24853.1; -.
 DR HSSP; P05067; 1HZ3.
 DR GO; GO:0016020; C:membrane; IEA.
 DR GO; GO:0004867; F:serine protease inhibitor activity; IEA.
 DR InterPro; IPR008155; A4_APP.
 DR InterPro; IPR008154; A4_extra.
 DR InterPro; IPR001255; Beta-APP.
 DR InterPro; IPR002223; Kunitz_BPTI.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR Pfam; PF03494; Beta-APP; 1.
 DR Pfam; PF00014; Kunitz_BPTI; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR PRINTS; PR00759; BASICPTASE.
 DR ProDom; PD000222; Kunitz_BPTI; 1.
 DR SMART; SM00131; KU; 1.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 DR PROSITE; PS00280; BPTI_KUNITZ_1; 1.
 DR PROSITE; PS50279; BPTI_KUNITZ_2; 1.
 KW Protease inhibitor; Serine protease inhibitor.
 SQ SEQUENCE 747 AA; 84893 MW; A75E81885681D948 CRC64;

Query Match 84.8%; Score 3095; DB 13; Length 747;
 Best Local Similarity 80.8%; Pred. No. 1.1e-177;
 Matches 596; Conservative 36; Mismatches 42; Indels 64; Gaps 5;

Qy	17	ALEVPTDGNAGLLAEPQIAMF-CGRLNMHMNVQNGKWSDPSGKTCTCIDTKEGILQYCQE	75
		:	
Db	15	ALEVLVDGNGLLAEPQIAMFSVARLNMHMNVQNGKWETDVSG---CIGTKEGILQYCQE	71
Qy	76	VYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDALLVPDKCKF	135
		: : :	
Db	72	VYPELQITNVVEANQPVTIQNWCKKGRKQCKSRTHIVVPYRCLVGEFVSDALLVPDKCKF	131
Qy	136	LHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVCCPLAEESDN	195
		: : : :	
Db	132	LHQERMDICETHLHWHTVAKESCSKMSLHEYGMLLPCGIDKFRGVEFVCCPSAEES	191
Qy	196	VDSADAEEDSDVWVGADTDYADGSEDKVVEVA---EEEEVAEVEEEEADDDDEDGDE	253
		:	
Db	192	FDSADAAEDDCDVWVGADADYVDRSDDKAVEAQPDEEEVVEVEEEEETDDDED--DGDE	249
Qy	254	VEEEAEEPVEEATERTTSIATTTTTTTTSEVEEVVR-----	288
Db	250	AEEPEEPVEEATERTTSIATTTTTTTTSEVEEVREVCSEQAETGPCRAMISRWYYDVTE	309
Qy	289	-----VPTTAASTPDAVDKYLETPGDENEHAHFQ	317
		:	
Db	310	SKCAQFIYGGCGGNRNNFESDDYCMVCGSVIPATAASTPDAVDKYLENPNDENEHDFL	369
Qy	318	KAKERLEAKHRERMSQVMREWEAERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQ	377
		: : : : : : : : : : : : : : : : : : :	
Db	370	KAKERLEGKHREKMSEVMKEWEAERQAKNLPKADKKAVIQHFQEKVESLEQEAQQRQQ	429

Qy	378	LVETHMARVEAMLNDRRRRLALENYITALQAVPPRPRHVFENMLKKYVRAEQKDRQHTLKHf	437
Db	430	LVETHMARVEAMLNDRRRRIALENYITALQADPPRPRHVFENMLKKYVRAEQKDRQHTLKHf	489
Qy	438	EHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQDEVDELLQKEQNY	497
Db	490	EHVRMVDPKKAAQIRSQVMTHLRVINERMNQSFSLLYKVPAAVEEIQDEVDELfQKEQNY	549
Qy	498	SDDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSLDDLQPPWHSFGADSVPAN	557
Db	550	SDDMVSNMVSdHRVSYGNDALMPSLSETKTTVELLPVDGEFNIEDLQPPWHSFGVDSVPAN	609
Qy	558	TENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEFRHDSGYEVHHQKLVFFA	617
Db	610	TENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDSEYRHDTAYEVHHQKLVFFA	669
Qy	618	EDVGSNKGAIIGLMVGGVVIATVIVITLVMKKKQYTSIHhGVVEVDAAVTPEERHLSKM	677
Db	670	EEVGSNKGAIIGLMVGGVVIATVIVITLVMKKKQYTTIHhGVVEVDAAVTPEERHLTKM	729
Qy	678	QQNGYENPTYKFFEQMQN	695
Db	730	OONGYENPTYKFFEQMON	747

057394

DR Pfam; PF03494; Beta-APP; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR SMART; SM00006; A4_EXTRA; 1.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 SQ SEQUENCE 699 AA; 78879 MW; 952915C309D50E5C CRC64;

Query Match 81.0%; Score 2956.5; DB 13; Length 699;
 Best Local Similarity 80.5%; Pred. No. 2.1e-169;
 Matches 567; Conservative 59; Mismatches 59; Indels 19; Gaps 8;

Qy 2 LPG-LALLLLAAWTA-----RALEVPTDGNAGLL-AEPQIAMFCGRLNMHMNVQNGKW 52
 ||| | :|||| | ||||| ||| |||||:||||:| | |||
 Db 5 LPGRLGMLLLAAAAALVLAPLCRALEVPTDGGAGLLAAEPQIAMFCGKLNMHVNVQTGKW 64

Qy 53 DSDPSGKTCTCIDTKEGILQYQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFV 112
 ||||| | |||||:|||||:|||||:|||||:||||| ||| |
 Db 65 VSDPSGTNTCFGTKEGILRYCQEVYPDLQITNVVEANQPITIQNWCKKGRKQCKGHPHIV 124

Qy 113 IPYRCLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLL 172
 :|||||:|||||:|||||:|||||:|||||:|||||:|||||
 Db 125 VPYRCLVGEFVSDALLVPDKCKFLHREKMDTCESHLYWHTVAKETCGDKIMNLHDYGMLL 184

Qy 173 PCGIDKFRGVFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEE 232
 |||||:|||||: ||:| || | :|:||||| | |||| | | | ||
 Db 185 PCGIDEFRGVFVCCPIPEENDKIDS-DMDEEDSDVWVGDDADYADGG-DKTV----EE 238

Qy 233 EVAEVEEEEEADDEDDEDGDEVEEE-AEPPYEEATERTTSIATTTTTTTTESVEEVVRVPT 291
 : | |||| : | |||| |:::| | : ||: || || | :|||||:|||||
 Db 239 KPIEEEEEEDESIDDEDDDDLDEVEDQYEDPTEHTTS---STTTTTEAIEEVVRVPT 295

Qy 292 TAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKA 351
 |||||:|||||:|||||:|||||:|||||:|||||:|||||
 Db 296 TAASTPDAVDKYLETPGDENEHAYFQKAKERLEAKHRERMSKIMREWEAAERQAKNLPKA 355

Qy 352 DKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRRLALENYITALQAVPPR 411
 ||||| ||| |||||:|||||:|||||:|||||:|||||: ||| |||
 Db 356 DKKAVIQRFQEMVESLEQEAASERQQLVETHMARVEAMLNDRRRIALENYLAALQADPPR 415

Qy 412 PRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLS 471
 |||| | |||| |||||:|||| | ||:||||:||||| || |||||
 Db 416 PRHVLNALKKYSRAEQKDRQHTLKHFDHVRVAVDPEKAAQIKSQVMTHLHVIDERMNQSLS 475

Qy 472 LLYNVPAAVEEQDEVDLLQKEQNYSDDLANMISEPRI SYGNDALMPSLTETKTTVEL 531
 ||| ||:|||||:|||||:|||||: ||: |||: |||||:|||||: ||
 Db 476 LLYKVPSVAEEIQDEVDLLQRRERSYMDMMANSVSDTRISYGNDALVPSLSETKTTIEL 535

Qy 532 LPVNGEFSDDLQPPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEI 591
 || :||| ||||| | | :|:|||||:||||| ||||| |||||
 Db 536 LPDDGEFILDDLQPPHPFVIESIPANTENEVEPVDARPAPDRGLTTRPGSGLTGKTEEI 595

Qy 592 SEVNLDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKK 651
 :|: :: ||: |||||:|||||:|||||:|||||:|||||:|||||
 Db 596 AELKMETEFQQDSGYEVHHQKLVFFPKDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKK 655

Qy 652 QYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
 |||||

09PVL1

```

ID      Q9PVL1          PRELIMINARY;          PRT;    569 AA.
AC      Q9PVL1;
DT      01-MAY-2000 (TrEMBLrel. 13, Created)
DT      01-MAY-2000 (TrEMBLrel. 13, Last sequence update)
DT      01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE      Amyloid protein (Fragment).
GN      APP.
OS      Gallus gallus (Chicken).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC      Gallus.
OX      NCBI_TaxID=9031;
RN      [1]
RP      SEQUENCE FROM N.A.
RC      TISSUE=Brain;
RA      Coulson E.J., Paliga K., Beyreuther K., Masters C.L.;
RT      "What the evolution of the amyloid protein precursor supergene family
RT      tells us about its function.";
RL      Neurochem. Int. 0:0-0(2000).
DR      EMBL; AF030341; AAF12698.1; -.
DR      HSSP; P05067; 1BA4.
DR      GO; GO:0016020; C:membrane; IEA.
DR      InterPro; IPR008155; A4_APP.
DR      InterPro; IPR008154; A4_extra.
DR      InterPro; IPR001255; Beta-APP.
DR      Pfam; PF02177; A4_EXTRA; 1.
DR      Pfam; PF03494; Beta-APP; 1.
DR      PRINTS; PR00203; AMYLOIDA4.
DR      PROSITE; PS00319; A4_EXTRA; 1.
DR      PROSITE; PS00320; A4_INTRA; 1.
FT      NON_TER          1          1
SQ      SEQUENCE    569 AA;  64753 MW;  0AB8BB851863A19D CRC64;

```

Query Match 75.6%; Score 2759.5; DB 13; Length 569;
Best Local Similarity 93.2%; Pred. No. 1.1e-157;
Matches 533; Conservative 15; Mismatches 19; Indels 5; Gaps 4;

Qy	126	ALLVDPDKCKFLHQERMDVCE	THLHWHTVAKETCSEKSTNL	HDYGMLLPCGIDKFRGVEFV	185
Db	1	ALLVDPDKCKLLHQERMDVCE	THLHWHTVAKESCSEKSMNL	HDYGMLLSCGIDKFRGVEFV	60
Qy	186	CCPLAEESDNVDSADAEE	DDSDVWVG	GADTDYADGSEDKVVE--VA	243
Db	61	CCPLAEESDNLDSADAED	DDSDVWVG	GADADYADGSDDKVVEEQPE	120
Qy	244	DDEDDGDGEVEEEAE	EPYEEATERTTSIAT	TTTTTTTTSVEEVVRVPTTA	303
Db	121	DD-DDDDGDEI-EETEE	EYEEATERTTSIAT	TTTTTTTTSVEEVVRVPTTA	178
Qy	304	LETPGDENEHAHFQKA	KERLEAKHRERMSQVM	REWEEAERQAKNLPKADK	363
Db	179	LETPGDENEHAHFQKA	KERLEAKHRERMSQVM	REWEEAERQAKNLPKADK	238

Qy 364 VESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYV 423
 |||:|||||
 Db 239 VESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQTVPPRPRHVFNMLKKYV 298

Qy 424 RAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEI 483
 |||:|||||
 Db 299 RAEQKDRQHTLKHFEHVRMVDPKKAVQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEI 358

Qy 484 QDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFLDDL 543
 |||:|||||
 Db 359 QDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPTLTETKTTVELLPVNGEFLDDL 418

Qy 544 QPWSHFGADSV PANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEFRHD 603
 |||||:|||:|
 Db 419 QPWHFPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTNVKTTEEVESEVKMDAEFRHD 478

Qy 604 SGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGHVVEV 663
 |||:|||||
 Db 479 SGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIANVIVITLVMLKKKQYTSIHGHVVEV 538

Qy 664 DAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
 |||||
 Db 539 DAAVTP-ERHLSKMQQNGYENPTYKFFEQMQN 569

RESULT 9

O93296

ID O93296 PRELIMINARY; PRT; 534 AA.
 AC O93296;
 DT 01-NOV-1998 (TrEMBLrel. 08, Created)
 DT 01-NOV-1998 (TrEMBLrel. 08, Last sequence update)
 DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
 DE Amyloid protein (Fragment).
 OS Gallus gallus (Chicken).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
 OC Gallus.
 OX NCBI_TaxID=9031;
 RN [1]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=98337885; PubMed=9671674;
 RA Barnes N.Y., Li L., Yoshikawa K., Schwartz L.M., Oppenheim R.W.,
 RA Milligan C.E.;
 RT "Increased production of amyloid precursor protein provides a
 RT substrate for caspase-3 in dying motoneurons."
 RL J. Neurosci. 18:5869-5880(1998).
 DR EMBL; AF042098; AAC25052.1; -.
 DR HSSP; P05067; 1BA4.
 DR GO; GO:0016020; C:membrane; IEA.
 DR InterPro; IPR008155; A4_APP.
 DR InterPro; IPR008154; A4_extra.
 DR InterPro; IPR001255; Beta-APP.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR Pfam; PF03494; Beta-APP; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR PROSITE; PS00319; A4_EXTRA; 1.

DR PROSITE; PS00320; A4_INTRA; 1.
FT NON_TER 1 1
SQ SEQUENCE 534 AA; 60597 MW; FB53ECC2E66D4C92 CRC64;

Query Match 71.4%; Score 2605; DB 13; Length 534;
Best Local Similarity 94.4%; Pred. No. 2e-148;
Matches 504; Conservative 14; Mismatches 12; Indels 4; Gaps 3;

```
Qy      164 NLHDYGMLLPCGIDKFRGVEFVCCPLAEESDNVDSADAEEEDSDVWVGADTDYADGSED 223
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      3  NLHDYGMLLPCGIDKFRGVEFVCCPLAEESDNLDSADAEDDDSDVWVGADADYADGSD 62

Qy      224 KVVE--VAEEEEVAEVEEEEADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTE 281
          ||||  |||: |||:|||| |||:|||| || || |||||:|||||:|||||:
Db      63 KVVEEQPEEDEELTVVEDEDADDD-DDDDGDEI-EETEEYEEATERTTSIATTTTTTTE 120

Qy      282 SVEEVVRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEA 341
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      121 SVEEVVRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEA 180

Qy      342 ERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRRLALENY 401
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      181 ERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRRIALENY 240

Qy      402 ITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRV 461
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      241 ITALQTVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRV 300

Qy      462 IYERMNQSLSLLYNVPAVAEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPS 521
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      301 IYERMNQSLSFLYNVPAVAEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPS 360

Qy      522 LTETKTTVELLPVNGEFSDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGS 581
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      361 LTETKTTVELLPVDGEFSDDLQPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGS 420

Qy      582 GLTNIKTEEISEVNLD AEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVI 641
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      421 GLTNVKTEEVSEVKMD AEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVI 480

Qy      642 VITLVMLKKKQYTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
          |||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:|||||:
Db      481 VITLVMLKKKQYTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 534
```

RESULT 10

Q7ZZT1

ID Q7ZZT1 PRELIMINARY; PRT; 678 AA.
AC Q7ZZT1;
DT 01-JUN-2003 (TrEMBLrel. 24, Created)
DT 01-JUN-2003 (TrEMBLrel. 24, Last sequence update)
DT 01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DE Amyloid protein a variant 2.
GN APPA.
OS Brachydanio rerio (Zebrafish) (Danio rerio).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;

OC Cyprinidae; Danio.
 OX NCBI_TaxID=7955;
 RN [1]
 RP SEQUENCE FROM N.A.
 RA Groth C., Lardelli M.;
 RT "Investigation of zebrafish appa expression during embryogenesis.";
 RL Submitted (APR-2003) to the EMBL/GenBank/DDBJ databases.
 DR EMBL; AY271746; AAP22958.1; -.
 DR GO; GO:0016020; C:membrane; IEA.
 DR InterPro; IPR008155; A4_APP.
 DR InterPro; IPR008154; A4_extra.
 DR InterPro; IPR001255; Beta-APP.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR Pfam; PF03494; Beta-APP; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR SMART; SM00006; A4_EXTRA; 1.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 SQ SEQUENCE 678 AA; 76755 MW; 94163778444FD0BC CRC64;

Query Match 70.2%; Score 2562; DB 13; Length 678;
 Best Local Similarity 71.9%; Pred. No. 1e-145;
 Matches 498; Conservative 78; Mismatches 95; Indels 22; Gaps 11;

Qy	5	LALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGKTCTCID	64
		: : : : :	
Db	6	LFILLMAVASTLAVEVPSDGTGLLAEPQIAMFCGKLNMHINIQSGKWEPPDPSGSKSCIG	65
Qy	65	TKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVS	124
Db	66	NKEGILQYCQEVYPELQITNVVEANQPVSIWDWCKKSRKQCRSHMHIVPYRCLVGEFVS	125
Qy	125	DALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEF	184
Db	126	DALLVPDKCKFLHQERMDMCESHLHWHTVAKESCGDRSMNLHDYGMLLPCGIDRFRGVEF	185
Qy	185	VCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEEEEEEADD	244
		: : : :	
Db	186	VCCP-ADAGKESESA AVEEDSDVWVGGA EADYTENSMTR--DAAAEP AV--LEDDEDAD	240
Qy	245	DEDDDEDGD-EVEEEAE EPYEEATERTT-SIATTTTTTTTESVEEVVRVPTTAASTPDAVDK	302
		: : : :	
Db	241	EEEDDEDGDGRDEKIEEEEEERTQSTSAALTSTTTTTTESVEEVVRVPTPSSSPDAVDR	300
Qy	303	YLET PGDENEHAHFQKAKERLEAKHRERMSQVMREWE EAERQAKNLPKADKKAVIQHFQE	362
Db	301	YLET PADENEHAHFLKAKESLET KHRERMSQVMREWE EAERQAKSLPRNDKKAVIQHFQE	360
Qy	363	KVESLEQE AANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKY	422
		: : :	
Db	361	KVEALEQESASERQQLVETHMARVEALLNDRRLALESYLSALQADPPRPRHVFSLKKY	420
Qy	423	VRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVAEE	482
Db	421	VRAEQKDRQHTLKHFEHVRMVDPKKAAQIRPQVLTHLRVIEERMNQSGLGLLYKVPGVADD	480
Qy	483	IQDEVDELLQKEQNYSDDVLANMISEPRI SYGNDALMPSLTETKTTVELLPVNGEFSLDD	542

```

ID Q90W28 PRELIMINARY; PRT; 738 AA.
AC Q90W28;
DT 01-DEC-2001 (TrEMBLrel. 19, Created)
DT 01-DEC-2001 (TrEMBLrel. 19, Last sequence update)
DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE Amyloid precursor protein.
GN APPA OR APP.
OS Brachydanio rerio (Zebrafish) (Danio rerio).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;
OC Cyprinidae; Danio.
OX NCBI_TaxID=7955;
RN [1]
RP SEQUENCE FROM N.A.
RA Groth C., Lardelli M.;
RT "Expression analysis of zebrafish app.";
RL Submitted (JUN-2001) to the EMBL/GenBank/DDBJ databases.
DR EMBL; AF389401; AAK64495.1; -.
DR ZFIN; ZDB-GENE-000616-13; appa.
DR GO; GO:0016020; C:membrane; IEA.
DR GO; GO:0004867; F:serine protease inhibitor activity; IEA.
DR InterPro; IPR008155; A4_APP.
DR InterPro; IPR008154; A4_extra.
DR InterPro; IPR001255; Beta-APP.
DR InterPro; IPR002223; Kunitz_BPTI.
DR Pfam; PF02177; A4_EXTRA; 1.
DR Pfam; PF03494; Beta-APP; 1.
DR Pfam; PF00014; Kunitz_BPTI; 1.
DR PRINTS; PR00203; AMYLOIDA4.
DR PRINTS; PR00759; BASICPTASE.
DR ProDom; PD000222; Kunitz_BPTI; 1.
DR SMART; SM00006; A4_EXTRA; 1.
DR SMART; SM00131; KU; 1.
DR PROSITE; PS00319; A4_EXTRA; 1.
DR PROSITE; PS00320; A4_INTRA; 1.
DR PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW Protease inhibitor; Serine protease inhibitor.
SQ SEQUENCE 738 AA; 83577 MW; AF480F6D308FD298 CRC64;

```

Query Match 69.1%; Score 2524; DB 13; Length 738;
Best Local Similarity 66.3%; Pred. No. 2.2e-143;
Matches 500; Conservative 79; Mismatches 91; Indels 84; Gaps 14;

```
Qy      5 LALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGKTCTCID 64
| :||:| : | :|||:| | ||||| :|||:| :|||: | |||:| :||
Db      6 LFILLMAVASTLAVEVPSDSTGLLAEPQIAMFCGKLMHINIQSGKWEPDPSGSKSCIG 65

Qy     65 TKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVGEFVS 124
| ||||| :|||:| |||:| | | :||| :|||:| | | :||| :|||
Db     66 NKEGILQYCQEVYPELQITNVVEANQPVSIWDWCKKSRKQCRSHMHIVVPIYRCLVGEFVS 125

Qy    125 DALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEF 184
| ||||| :|||:| |||:| | | :||| :|||:| | | :||| :|||
Db    126 DALLVPDKCKFLHQERMDMCESHLHWHTVAKESCGDRSMNLHDYGMLLPCGIDRFRGVEF 185

Qy    185 VCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEEEADD 244
| ||| | : :|| | ||||| :|| :| : :| | | :|||:| :||
Db    186 VCCP-ADAGKESESA AVEEDSDVWWGGAEADYTENSMT--DAAAEPAVLE-DDEDADE 241

Qy    245 DED-DEDGD-----EVEEEAEPEYEEATERTT-SIATTTTTTTTESVEEVVR----- 288
: || | :||| :||| || || | : | : : : ||||| :|||
Db    242 EEDEDQDGDGDRDEKIEEEEE--EERTQSTSAALTSTTTTTTESVEEVVREVCFASAET 299

Qy    289 -----VPTTAASTPDAVD 301
: || :|| ||||
Db    300 GPCRAMLRSWYYVREERRCAPFIYGGCGGNRNNFESEYCLSVCSGVLPTPSSSPDAVD 359

Qy    302 KYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQ 361
: |||| | ||||| |||| || | ||||| :||| : |||||
Db    360 RYLETPADENEHAHFLKAKESLETKHRERMSQVMREWEEAERQAKSLPRNDKKAVIQHFQ 419

Qy    362 EKVESLEQEAAANERQQVLVETHMARVEAMLNDRRRLALENYITALQAVPPRPRHVFENMLKK 421
| |||:| |||:| :||| :|||:| |||:| | | :||| :|||
Db    420 EKVEALEQESASERQQVLVETHMARVEALLNDRRRLALESYLSALQADPPRPRHVFSLKK 479

Qy    422 YVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVAE 481
| ||||| :|||:| |||:| | | :||| :|||:| |||:| |||:| |||:|
Db    480 YVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRPQVLTHLRVIEERMNQSGLLYKVPGVAD 539

Qy    482 EIQDEVDELLQKEQNYSDDLANMISEPRISYGNDALMPSLTETKTTVELLPVNGEFSLD 541
: |||:| |||:| |||:| | | :||| :|||:| | | :|||
Db    540 DIQDQV-ELLQREQQEMSAQLANLQSDARVSYGNDALMPDST---AGLELLPAEDTQGFG 595

Qy    542 DLQPWHSFGADSVPAANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEFR 601
: | || | | :||| :|||:| | | ||| ||| :|| :| :|||
Db    596 FIHP-ESFN---QPNTHNQVEPVDARVPDLDLATRPVSGL---KPDDIPELRMEAEER 647

Qy    602 HDSGYEVVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGV 661
| | :||| :|||:| |||:| | | :||| :|||:| |||:| |||:|
Db    648 HS---EVYHQKLVFFAEDVSSNKGAIIGLMVGGVVIATIIIVITLVMLRKKQYTSIHGGII 704

Qy    662 EVDAAVTPEERHLSKMQQNGYENPTYKFFEQM 695
| ||||| :|||:| |||:| | | :|||
Db    705 EVDAAVTPEERHLSKMQQNGYENPTYKFFEQMHN 738
```

RESULT 12

Q8UUR9

ID Q8UUR9 PRELIMINARY; PRT; 694 AA.
AC Q8UUR9;
DT 01-MAR-2002 (TrEMBLrel. 20, Created)
DT 01-MAR-2002 (TrEMBLrel. 20, Last sequence update)
DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE Putative membrane protein.
GN APPB.
OS Brachydanio rerio (Zebrafish) (Danio rerio).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;
OC Cyprinidae; Danio.
OX NCBI_TaxID=7955;
RN [1]
RP SEQUENCE FROM N.A.
RC TISSUE=Brain;
RX PubMed=11862463;
RA Musa A., Lehrach H., Russo V.E.A.;
RT "Distinct expression patterns of two zebrafish homologues of the human
RT APP gene during embryonic development.";
RL Dev. Genes Evol. 211:563-567(2001).
DR EMBL; AJ315639; CAC85736.1; -.
DR ZFIN; ZDB-GENE-020220-1; appb.
DR GO; GO:0016020; C:membrane; IEA.
DR InterPro; IPR008155; A4_APP.
DR InterPro; IPR008154; A4_extra.
DR InterPro; IPR001255; Beta-APP.
DR Pfam; PF02177; A4_EXTRA; 1.
DR Pfam; PF03494; Beta-APP; 1.
DR PRINTS; PR00203; AMYLOIDA4.
DR SMART; SM00006; A4_EXTRA; 1.
DR PROSITE; PS00319; A4_EXTRA; 1.
DR PROSITE; PS00320; A4_INTRA; 1.
SQ SEQUENCE 694 AA; 79228 MW; 2B03382D411162DC CRC64;

Query Match 68.1%; Score 2487.5; DB 13; Length 694;
Best Local Similarity 68.0%; Pred. No. 3.2e-141;
Matches 478; Conservative 96; Mismatches 98; Indels 31; Gaps 9;

Qy 7 LLLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWSDPSGKTCTIDTK 66
| | | : : | : | | : | : | | | | : | | | : | | : | | : | | : | | : | |
Db 9 LLLMLTTLSLAIEVPSDDSVGLLAEPQVAMFCGKLNMHINVQSGKWEPTDPTGKSCISTK 68
Qy 67 EGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDA 126
| | | : | | | | : | | | | | | | | | | | | | | | | | : | | : : | | : | | | | | | | |
Db 69 EGILKYCQEVYPDLQITNVVEANQPVSIQNWCKMGRRQCRSHTHIVVPYRCLVGEFVSDA 128
Qy 127 LLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVC 186
| | | | | | | | | | | | : | | : | | | | | | | : : | | | | | | | | | | | | | | | | |
Db 129 LLVPDKCKFLHQERMDMCESHLHWHTVAKESCGDRSMNLHDYGMLLPCGIDRFRGVEFVC 188
Qy 187 CPLAEESDNVDSADAEEDSDVWVGADTDYADGS--EDKVV-----EVAEEEEVAEVEE 239
| | : | : | : | | : | | : | | | | | : | | : : | | : | | : | |
Db 189 CPMEEQKD-LDSEEQEEANSDVWVGGAETEYTDASVLKEQVTAKPDPAVTEDEDLNEE 247

O8BPC7

Query Match 52.6%; Score 1920; DB 11; Length 384;
Best Local Similarity 97.7%; Pred. No. 1.8e-107;
Matches 375; Conservative 3; Mismatches 6; Indels 0; Gaps 0;

Qy	312	EHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEKVESLEQEA	371
Db	1	EHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEKVESLEQEA	60
Qy	372	ANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPHVFNMLKKYVRAEQKDRQ	431
Db	61	ANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPHVFNMLKKYVRAEQKDRQ	120
Qy	432	HTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQDEVDELL	491
Db	121	HTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQDEVDELL	180
Qy	492	QKEQNYSDVDLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSLDDLQPWHSFGA	551
Db	181	QKEQNHSDDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSLDDLQPWHPFGV	240
Qy	552	DSVPANTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEFRHDSGYEVHHQ	611

Db 241 DSVPA NTENEVEPVDARPAADRGLTTRPGSGLTNIKTEEISEVKMDAEFGHDSGFVVRHQ 300

Qy 612 KLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGVVEVDAAVTPEE 671
 |||

Db 301 KLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGGVVEVDAAVTPEE 360

Qy 672 RHL SKMQQNGYENPTYKFFEQMQN 695
 |||

Db 361 RHL SKMQQNGYENPTYKFFEQMQN 384

RESULT 15

Q13861

ID Q13861 PRELIMINARY; PRT; 695 AA.

AC Q13861;

DT 01-NOV-1996 (TrEMBLrel. 01, Created)

DT 01-NOV-1996 (TrEMBLrel. 01, Last sequence update)

DT 01-JUN-2003 (TrEMBLrel. 24, Last annotation update)

DE Binding protein (Fragment).

OS Homo sapiens (Human).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

OX NCBI_TaxID=9606;

RN [1]

RP SEQUENCE FROM N.A.

RC TISSUE=Brain;

RA Vostrov A.A., Quitschke W.W., Schwarzman A.L., Blangy A., Cuzin F.,

RA Wesley U.V., Hagag N.G., Goldgaber D.;

RT "Cloning of a protein that binds to a recognition sequence in the APP

RT promoter.";

RL Submitted (JUN-1993) to the EMBL/GenBank/DDBJ databases.

DR EMBL; L19597; AAA35601.1; -.

DR HSSP; P05067; 1MWP.

DR InterPro; IPR008155; A4_APP.

DR InterPro; IPR008154; A4_extra.

DR Pfam; PF02177; A4_EXTRA; 1.

DR PRINTS; PR00203; AMYLOIDA4.

DR SMART; SM00006; A4_EXTRA; 1.

DR PROSITE; PS00319; A4_EXTRA; 1.

DR PROSITE; PS00320; A4_INTRA; 1.

FT NON_TER 1 1

FT NON_TER 695 695

SQ SEQUENCE 695 AA; 79238 MW; 728CA8ACBB7594FB CRC64;

Query Match 48.3%; Score 1762; DB 4; Length 695;

Best Local Similarity 50.8%; Pred. No. 1.2e-97;

Matches 366; Conservative 113; Mismatches 171; Indels 70; Gaps 17;

Qy 5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWSDP 56
 | ||| || || : ||| : ||| ||| ||| ||| ||| ||| ||| ||| |||

Db 15 LLLLLLVGLTAPALALAGYIEALAANAGTGFAVAEPQIAMFCGKLNMHVNIQTGKWEPPD 74

Qy 57 SGTKTCTIDTKEGILQYCYEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
 : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : ||| : |||

Db 75 TGTKSCFETKEEVLYCYQEMPELQITNVMEANQRVSIDNWCRRDKKQCKS--RFVTPFK 132

Qy 117 CLVGEFVSDALLVDPKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176

Db	133	CLVGEFVSDVLLVPEKQFFHKERMEVCENHQHWHTVVKEACLTQGMTLYSYGMLLPCGV	192
Qy	177	DKFRGVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAE	236
Db	193	DQFHGTEYVCCPQTKIIGSVSKEEEEEDEE-----EEEEDEEEDYDVYKSEFPTEAD	245
Qy	237	VEE--EEA--DDDEDDGDEVEEEAE-----EPYEEATERTTSIATTTTTTTESVE	284
Db	246	LEDFTAAVDEDEDEEEGEEVVEDRDYDYDTFKGDDYNE--ENPTEPGSDGTMSDKEIT	303
Qy	285	EVVRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQ	344
Db	304	HDVKVPPTPLPTND--VDVYFETSADDNEHARFQKAKEQLEIRHRNRMDRVKKEWEEAELQ	362
Qy	345	AKNLPKADKKAVIQHFQEKVESLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITA	404
Db	363	AKNLPKAERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRRMALENYLAA	422
Qy	405	LQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYE	464
Db	423	LQSDPPRPHRILQALRRYVRAENKDLRHTIRHYQHVLAVDPEKAAQMKSQVMTHLHVIEE	482
Qy	465	RMNQSLSLLYNVPAAVEEIQDEVDLLEQEQNYSDVLNMISEPRISYGNLMPSLTE	524
Db	483	RRNQSLSLLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTASISE	525
Qy	525	TKTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDPARPAADRGL-----	575
Db	526	TPVDVR---VSSEES-EEIPPFHPF--HPFPALPENEGSGVGEQ---DGGLIGAEKVIN	576
Qy	576	-TTRPGSGLTNIKTEEISEVNLDAEFRHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGG	634
Db	577	SKNKVDENMVIDETLDVKEMI FNAE--RVGGLEERESVGPLREDFSLSSSALIGLLVIA	634
Qy	635	VVIATVIVITLVMLKKKQYTSIHGVEVDAAVTPEERHLSKMQONGYENPTYKFFEQMQ	694
Db	635	VAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQNHYENPTYKYLEQMQ	694

Search completed: July 26, 2004, 12:46:34
Job time : 36.3333 secs

OM protein - protein search, using sw model

Run on: July 26, 2004, 12:39:28 ; Search time 9 Seconds
(without alignments)
4032.544 Million cell updates/sec

Title: US-09-806-194A-18
Perfect score: 3651
Sequence: 1 MLPGLALLLLAAWTARALEV.....QQNGYENPTYKFFEQMQNKK 697

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 141681 seqs, 52070155 residues

Total number of hits satisfying chosen parameters: 141681

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : SwissProt_42:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query		DB	ID	Description
		Match	Length			
1	3582.5	98.1	770	1	A4_HUMAN	P05067 h amyloid b
2	3582.5	98.1	770	1	A4_MACFA	P53601 m amyloid b
3	3576	97.9	751	1	A4_SAISC	Q95241 s amyloid b
4	3527.5	96.6	770	1	A4_PIG	P79307 s amyloid b
5	3514.5	96.3	770	1	A4_CAVPO	Q60495 c amyloid b
6	3485.5	95.5	770	1	A4_MOUSE	P12023 m amyloid b
7	3485.5	95.5	770	1	A4_RAT	P08592 r amyloid b
8	2568	70.3	780	1	A4_TETFL	O73683 tetraodon f
9	2446.5	67.0	737	1	A4_FUGRU	O93279 fugu rubrip
10	1730	47.4	695	1	APP2_MOUSE	Q06335 mus musculu
11	1725	47.2	763	1	APP2_HUMAN	Q06481 homo sapien
12	1709	46.8	765	1	APP2_RAT	P15943 rattus norv
13	1191	32.6	650	1	APP1_HUMAN	P51693 homo sapien
14	1183	32.4	653	1	APP1_MOUSE	Q03157 mus musculu
15	815.5	22.3	686	1	A4_CAEL	Q10651 caenorhabdi
16	747.5	20.5	887	1	A4_DROME	P14599 drosophila
17	284	7.8	59	1	A4_BOVIN	Q28053 bos taurus

18	280	7.7	58	1	A4_RABIT	Q28748	oryctolagus
19	280	7.7	58	1	A4_SHEEP	Q28757	ovis aries
20	279	7.6	58	1	A4_CANFA	Q28280	canis famil
21	275	7.5	57	1	A4_URUMA	Q29149	ursus marit
22	185.5	5.1	407	1	IE68_HSVSA	Q01042	herpesvirus
23	185.5	5.1	993	1	SCP1_MOUSE	Q62209	mus musculu
24	176	4.8	2004	1	MYS3_HUMAN	Q92794	homo sapien
25	175.5	4.8	802	1	NAB3_YEAST	P38996	saccharomyc
26	171.5	4.7	793	1	CALD_HUMAN	Q05682	homo sapien
27	170	4.7	1498	1	GOA3_HUMAN	Q08378	homo sapien
28	169.5	4.6	297	1	TRT2_HUMAN	P45379	homo sapien
29	169.5	4.6	1875	1	MLP1_YEAST	Q02455	saccharomyc
30	169	4.6	771	1	CALD_CHICK	P12957	gallus gall
31	168	4.6	721	1	YCF2_OENPI	P31568	oenothera p
32	167.5	4.6	816	1	YG3A_YEAST	P53278	saccharomyc
33	167	4.6	1240	1	YNJ1_YEAST	P53935	saccharomyc
34	166.5	4.6	681	1	MP10_HUMAN	O00566	homo sapien
35	164	4.5	2017	1	MYSN_DROME	Q99323	drosophila
36	163.5	4.5	1976	1	MYHA_HUMAN	P35580	homo sapien
37	162.5	4.5	712	1	NUCL_RAT	P13383	rattus norv
38	162.5	4.5	1332	1	SPT7_YEAST	P35177	saccharomyc
39	162.5	4.5	1447	1	GOA3_MOUSE	P55937	mus musculu
40	161.5	4.4	1976	1	MYHA_RAT	Q9jlt0	rattus norv
41	160.5	4.4	1955	1	PUMA_PARUN	O61308	parascaris
42	158	4.3	301	1	TRT2_CHICK	P02642	gallus gall
43	157.5	4.3	1976	1	MYHA_BOVIN	Q27991	bos taurus
44	157	4.3	706	1	NUCL_HUMAN	P19338	homo sapien
45	156.5	4.3	5596	1	MDN1_HUMAN	Q9nu22	homo sapien

ALIGNMENTS

RESULT 1

A4_HUMAN

ID A4_HUMAN STANDARD; PRT; 770 AA.

AC P05067; P09000; P78438; Q13764; Q13778; Q13793; Q16011; Q16014;

AC Q16019; Q16020; Q9BT38; Q9UCA9; Q9UCB6; Q9UCC8; Q9UCD1; Q9UQ58;

DT 13-AUG-1987 (Rel. 05, Created)

DT 01-NOV-1991 (Rel. 20, Last sequence update)

DT 15-MAR-2004 (Rel. 43, Last annotation update)

DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease

DE amyloid protein) (Cerebral vascular amyloid peptide) (CVAP) (Protease

DE nexin-II) (PN-II) (APPI) (PreA4) [Contains: Soluble APP-alpha (S-APP-

DE alpha); Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42

DE (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42);

DE P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59)

DE (Amyloid intracellular domain 59) (AID(59)); Gamma-CTF(57) (Gamma-

DE secretase C-terminal fragment 57) (Amyloid intracellular domain 57)

DE (AID(57)); Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50)

DE (Amyloid intracellular domain 50) (AID(50)); C31].

GN APP OR A4 OR AD1.

OS Homo sapiens (Human).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

OX NCBI_TaxID=9606;

RN [1]

RP SEQUENCE FROM N.A. (ISOFORM APP695).
 RC TISSUE=Brain;
 RX MEDLINE=87144572; PubMed=2881207;
 RA Kang J., Lemaire H.-G., Unterbeck A., Salbaum J.M., Masters C.L.,
 RA Grzeschik K.-H., Multhaup G., Beyreuther K., Mueller-Hill B.;
 RT "The precursor of Alzheimer's disease amyloid A4 protein resembles a
 RT cell-surface receptor.";
 RL Nature 325:733-736(1987).
 RN [2]

RP SEQUENCE FROM N.A. (ISOFORM APP751).
 RC TISSUE=Brain;
 RX MEDLINE=88122639; PubMed=2893289;
 RA Ponte P., Gonzalez-Dewhitt P., Schilling J., Miller J., Hsu D.,
 RA Greenberg B., Davis K., Wallace W., Lieberburg I., Fuller F.,
 RA Cordell B.;
 RT "A new A4 amyloid mRNA contains a domain homologous to serine
 RT proteinase inhibitors.";
 RL Nature 331:525-527(1988).
 RN [3]

RP SEQUENCE FROM N.A. (ISOFORM APP695).
 RX MEDLINE=89128427; PubMed=2783775;
 RA Lemaire H.-G., Salbaum J.M., Multhaup G., Kang J., Bayney R.M.,
 RA Unterbeck A., Beyreuther K., Mueller-Hill B.;
 RT "The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid
 RT is encoded by 16 exons.";
 RL Nucleic Acids Res. 17:517-522(1989).
 RN [4]

RP SEQUENCE FROM N.A. (ISOFORM APP770).
 RX MEDLINE=90236318; PubMed=2110105;
 RA Yoshikai S.-I., Sasaki H., Doh-Ura K., Furuya H., Sakaki Y.;
 RT "Genomic organization of the human amyloid beta-protein precursor
 RT gene.";
 RL Gene 87:257-263(1990).
 RN [5]

RP ERRATUM, AND REVISIONS.
 RA Yoshikai S.-I., Sasaki H., Doh-ura K., Furuya H., Sakaki Y.;
 RL Gene 102:291-292(1991).
 RN [6]

RP SEQUENCE FROM N.A. (ISOFORM L-APP733).
 RC TISSUE=Leukocyte;
 RX MEDLINE=92268136; PubMed=1587857;
 RA Koenig G., Moenning U., Czech C., Prior R., Banati R.,
 RA Schreiter-Gasser U., Bauer J., Masters C.L., Beyreuther K.;
 RT "Identification and differential expression of a novel alternative
 RT splice isoform of the beta A4 amyloid precursor protein (APP) mRNA in
 RT leukocytes and brain microglial cells.";
 RL J. Biol. Chem. 267:10804-10809(1992).
 RN [7]

RP SEQUENCE FROM N.A. (ISOFORM APP770).
 RX MEDLINE=97263807; PubMed=9108164;
 RA Hattori M., Tsukahara F., Furuhashi Y., Tanahashi H., Hirose M.,
 RA Saito M., Tsukuni S., Sakaki Y.;
 RT "A novel method for making nested deletions and its application for
 RT sequencing of a 300 kb region of human APP locus.";
 RL Nucleic Acids Res. 25:1802-1808(1997).
 RN [8]

RP SEQUENCE FROM N.A. (ISOFORM APP639).

RC TISSUE=Brain;
 RX MEDLINE=22744650; PubMed=12859342;
 RA Tang K., Wang C., Shen C., Sheng S., Ravid R., Jing N.;
 RT "Identification of a novel alternative splicing isoform of human
 RT amyloid precursor protein gene, APP639.";
 RL Eur. J. Neurosci. 18:102-108(2003).
 RN [9]
 RP SEQUENCE FROM N.A. (ISOFORM APP305).
 RC TISSUE=Pancreas;
 RX MEDLINE=22388257; PubMed=12477932;
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
 RT "Generation and initial analysis of more than 15,000 full-length
 RT human and mouse cDNA sequences.";
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
 RN [10]
 RP SEQUENCE OF 1-10 FROM N.A.
 RC TISSUE=Liver;
 RX MEDLINE=89016647; PubMed=3140222;
 RA Schon E.A., Mita S., Sadlock J., Herbert J.;
 RT "A cDNA specifying the human amyloid beta precursor protein (ABPP)
 RT encodes a 95-kDa polypeptide.";
 RL Nucleic Acids Res. 16:9351-9351(1988).
 RN [11]
 RP ERRATUM, AND REVISIONS.
 RA Mita S., Sadlock J., Herbert J., Schon E.A.;
 RL Nucleic Acids Res. 16:11402-11402(1988).
 RN [12]
 RP SEQUENCE OF 1-75 FROM N.A.
 RX MEDLINE=89165870; PubMed=2538123;
 RA La Fauci G., Lahiri D.K., Salton S.R., Robakis N.K.;
 RT "Characterization of the 5'-end region and the first two exons of the
 RT beta-protein precursor gene.";
 RL Biochem. Biophys. Res. Commun. 159:297-304(1989).
 RN [13]
 RP SEQUENCE OF 18-50.
 RC TISSUE=Fibroblast;
 RX MEDLINE=87250462; PubMed=3597385;
 RA van Nostrand W.E., Cunningham D.D.;
 RT "Purification of protease nexin II from human fibroblasts.";
 RL J. Biol. Chem. 262:8508-8514(1987).
 RN [14]

RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP751).
 RC TISSUE=Brain;
 RX MEDLINE=89346754; PubMed=2569763;
 RA de Sauvage F., Octave J.N.;
 RT "A novel mRNA of the A4 amyloid precursor gene coding for a possibly
 RT secreted protein.";
 RL Science 245:651-653(1989).
 RN [15]
 RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP695).
 RC TISSUE=Brain;
 RX MEDLINE=87231971; PubMed=3035574;
 RA Robakis N.K., Ramakrishna N., Wolfe G., Wisniewski H.M.;
 RT "Molecular cloning and characterization of a cDNA encoding the
 RT cerebrovascular and the neuritic plaque amyloid peptides.";
 RL Proc. Natl. Acad. Sci. U.S.A. 84:4190-4194(1987).
 RN [16]
 RP SEQUENCE OF 286-366 FROM N.A.
 RX MEDLINE=88122640; PubMed=2893290;
 RA Tanzi R.E., McClatchey A.I., Lamperti E.D., Villa-Komaroff L.,
 RA Gusella J.F., Neve R.L.;
 RT "Protease inhibitor domain encoded by an amyloid protein precursor
 RT mRNA associated with Alzheimer's disease.";
 RL Nature 331:528-530(1988).
 RN [17]
 RP SEQUENCE OF 287-367 FROM N.A.
 RX MEDLINE=88122641; PubMed=2893291;
 RA Kitaguchi N., Takahashi Y., Tokushima Y., Shiojiri S., Ito H.;
 RT "Novel precursor of Alzheimer's disease amyloid protein shows
 RT protease inhibitory activity.";
 RL Nature 331:530-532(1988).
 RN [18]
 RP SEQUENCE OF 507-770 FROM N.A.
 RC TISSUE=Brain cortex;
 RX MEDLINE=88124954; PubMed=2893379;
 RA Zain S.B., Salim M., Chou W.G., Sajdel-Sulkowska E.M., Majocha R.E.,
 RA Marotta C.A.;
 RT "Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer
 RT disease brain: coding and noncoding regions of the fetal precursor
 RT mRNA are expressed in the cortex.";
 RL Proc. Natl. Acad. Sci. U.S.A. 85:929-933(1988).
 RN [19]
 RP SEQUENCE OF 523-555, AND COLLAGEN-BINDING DOMAIN.
 RX MEDLINE=96139497; PubMed=8576160;
 RA Behr D., Hesse L., Masters C.L., Multhaup G.;
 RT "Regulation of amyloid protein precursor (APP) binding to collagen and
 RT mapping of the binding sites on APP and collagen type I.";
 RL J. Biol. Chem. 271:1613-1620(1996).
 RN [20]
 RP SEQUENCE OF 655-737 FROM N.A., AND VARIANTS AD PHE-717; AD ILE-717
 RP AND AD GLY-717.
 RX MEDLINE=93236601; PubMed=8476439;
 RA Denman R.B., Rosenzwaig R., Miller D.L.;
 RT "A system for studying the effect(s) of familial Alzheimer disease
 RT mutations on the processing of the beta-amyloid peptide precursor.";
 RL Biochem. Biophys. Res. Commun. 192:96-103(1993).
 RN [21]
 RP SEQUENCE OF 656-737 FROM N.A.

RX MEDLINE=89392030; PubMed=2675837;
RA Johnstone E.M., Chaney M.O., Moore R.E., Ward K.E., Norris F.H.,
RA Little S.P.;
RT "Alzheimer's disease amyloid peptide is encoded by two exons and shows
RT similarity to soybean trypsin inhibitor.";
RL Biochem. Biophys. Res. Commun. 163:1248-1255(1989).
RN [22]

Query Match 98.1%; Score 3582.5; DB 1; Length 770;
Best Local Similarity 89.9%; Pred. No. 1.8e-168;
Matches 692; Conservative 2; Mismatches 1; Indels 75; Gaps 1;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPIYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Db	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVR-----	288
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVREVCSEQAETGPC	300
Qy	289	-----	288
Db	301	RAMISRWFYFDVTEGKCAPFFYGGCGGNRNFDTEEYCMVCGSAMSQSLLKTTQEPLARD	360
Qy	289	---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA	345
		:	
Db	361	PVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA	420
Qy	346	KNLPKADKKAVIQHFQEKVESLEQEAAERQQLVETHMARVEAMLNDRRRLALENYITAL	405
Db	421	KNLPKADKKAVIQHFQEKVESLEQEAAERQQLVETHMARVEAMLNDRRRLALENYITAL	480
Qy	406	QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	465
Db	481	QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	540
Qy	466	MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTET	525
Db	541	MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTET	600
Qy	526	KTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN	585
Db	601	KTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN	660
Qy	586	IKTEEISEVNLDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL	645

```

Db      661 IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 720
Qy      646 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
Db      721 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 770

```

RESULT 2

A4_MACFA

```

ID      A4_MACFA          STANDARD;          PRT;          770 AA.
AC      P53601; Q95KN7;
DT      01-OCT-1996 (Rel. 34, Created)
DT      28-FEB-2003 (Rel. 41, Last sequence update)
DT      28-FEB-2003 (Rel. 41, Last annotation update)
DE      Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE      amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE      Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-
DE      APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);
DE      Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE      (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE      secretase C-terminal fragment 50); C31].
GN      APP.
OS      Macaca fascicularis (Crab eating macaque) (Cynomolgus monkey).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Mammalia; Eutheria; Primates; Catarrhini; Cercopithecidae;
OC      Cercopithecinae; Macaca.
OX      NCBI_TaxID=9541;
RN      [1]
RP      SEQUENCE FROM N.A. (ISOFORMS APP695 AND APP770).
RC      TISSUE=Cerebellum;
RX      MEDLINE=91273117; PubMed=1905108;
RA      Podlisny M.B., Tolan D.R., Selkoe D.J.;
RT      "Homology of the amyloid beta protein precursor in monkey and human
RT      supports a primate model for beta amyloidosis in Alzheimer's
RT      disease.";
RL      Am. J. Pathol. 138:1423-1435(1991).
CC      -!- FUNCTION: Functions as a cell surface receptor and performs
CC      physiological functions on the surface of neurons relevant to
CC      neurite growth, neuronal adhesion and axonogenesis. Involved in
CC      cell mobility and transcription regulation through protein-protein
CC      interactions (By similarity). Can promote transcription activation
CC      through binding to APBB1/Tip60 and inhibit Notch signaling through
CC      interaction with Numb (By similarity). Couples to apoptosis-
CC      inducing pathways such as those mediated by G(0) and JIP (By
CC      similarity). Inhibits G(0) alpha ATPase activity (By similarity).
CC      Acts as a kinesin I membrane receptor, mediating the axonal
CC      transport of beta-secretase and presenilin 1 (By similarity). May
CC      be involved in copper homeostasis/oxidative stress through copper
CC      ion reduction. In vitro, copper-metallated APP induces neuronal
CC      death directly or is potentiated through Cu(II)-mediated low-
CC      density lipoprotein oxidation (By similarity). Can regulate
CC      neurite outgrowth through binding to components of the
CC      extracellular matrix such as heparin and collagen I and IV (By
CC      similarity). The splice isoforms that contain the BPTI domain
CC      possess protease inhibitor activity (By similarity).
CC      -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators

```

with metal-reducing activity. Bind transient metals such as copper, zinc and iron (By similarity).

FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved peptides, including C31, are potent enhancers of neuronal apoptosis (By similarity).

SUBUNIT: Binds, via its C-terminal, to the PID domain of several cytoplasmic proteins, including APBB family members, the APBA family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding to Dab1 inhibits its serine phosphorylation (By similarity). Also interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2 (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1. In vitro, it binds MAPT via the MT-binding domains (By similarity). Associates with microtubules in the presence of ATP and in a kinesin-dependent manner (By similarity).

SUBCELLULAR LOCATION: Type I membrane protein. Cell surface protein that rapidly becomes internalized via clathrin-coated pits. During maturation, the immature APP (N-glycosylated in the endoplasmic reticulum) moves to the Golgi complex where complete maturation occurs (O-glycosylated and sulfated). After alpha-secretase cleavage, soluble APP is released into the extracellular space and the C-terminal is internalized to endosomes and lysosomes. Some APP accumulates in secretory transport vesicles leaving the late Golgi compartment and returns to the cell surface. Gamma-CTF(59) peptide is located to both the cytoplasm and nuclei of neurons (By similarity).

ALTERNATIVE PRODUCTS:

Event=Alternative splicing; Named isoforms=2;
Comment=Additional isoforms seem to exist;
Name=APP770;
IsoId=P53601-1; Sequence=Displayed;
Name=APP695;
IsoId=P53601-2; Sequence=VSP_000010, VSP_000011;

DOMAIN: The basolateral sorting signal (BaSS) is required for sorting of membrane proteins to the basolateral surface of epithelial cells (By similarity).

DOMAIN: The NPXY sequence motif found in many tyrosine-phosphorylated proteins is required for the specific binding of the PID domain. However additional amino acids either N- or C-terminal to the NPXY motif are often required for complete interaction. The PID domain-containing proteins which bind APP require the YENPTY motif for full interaction. These interactions are independent of phosphorylation on the terminal tyrosine residue. The NPXY site is also involved in clathrin-mediated endocytosis (By similarity).

PTM: Proteolytically processed under normal cellular conditions. Cleavage by alpha-secretase or alternatively by beta-secretase leads to generation and extracellular release of soluble APP peptides, S-APP-alpha and S-APP-beta, respectively, and the retention of corresponding membrane-anchored C-terminal fragments, C83 and C99. Subsequent processing of C83 by gamma-secretase yields P3 peptides. This is the major secretory pathway and is nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated gamma-secretase processing of C99 releases the amyloid beta proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42), major components of amyloid plaques, and the cytotoxic C-terminal fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By similarity).

CC -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis
 CC (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9
 CC results in the production of the neurotoxic C31 peptide and the
 CC increased production of beta-amyloid peptides (By similarity).
 CC -!- PTM: N- and O-glycosylated (By similarity).
 CC -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
 CC serine residues is neuron-specific. Phosphorylation can affect APP
 CC processing, neuronal differentiation and interaction with other
 CC proteins (By similarity).
 CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
 CC zinc, can induce histidine-bridging between beta-amyloid molecules
 CC resulting in beta-amyloid-metal aggregates (By similarity).
 CC Extracellular zinc-binding increases binding of heparin to APP and
 CC inhibits collagen-binding (By similarity).
 CC -!- SIMILARITY: Belongs to the APP family.
 CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

CC -----
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
 CC the European Bioinformatics Institute. There are no restrictions on its
 CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by and for commercial
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
 CC or send an email to license@isb-sib.ch).
 CC -----

DR EMBL; M58727; AAA36829.1; -.
 DR EMBL; M58726; AAA36828.1; -.
 DR HSSP; P05067; 1AAP.
 DR InterPro; IPR008155; A4_APP.
 DR InterPro; IPR008154; A4_extra.
 DR InterPro; IPR001255; Beta-APP.
 DR InterPro; IPR002223; Kunitz_BPTI.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR Pfam; PF03494; Beta-APP; 1.
 DR Pfam; PF00014; Kunitz_BPTI; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR PRINTS; PR00759; BASICPTASE.
 DR ProDom; PD000222; Kunitz_BPTI; 1.
 DR SMART; SM00006; A4_EXTRA; 1.
 DR SMART; SM00131; KU; 1.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 DR PROSITE; PS00280; BPTI_KUNITZ_1; 1.
 DR PROSITE; PS50279; BPTI_KUNITZ_2; 1.
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
 KW Proteoglycan; Alternative splicing; Amyloid.
 FT SIGNAL 1 17 BY SIMILARITY.
 FT CHAIN 18 770 AMYLOID BETA A4 PROTEIN.
 FT CHAIN 18 687 SOLUBLE APP-ALPHA (POTENTIAL).
 FT CHAIN 18 671 SOLUBLE APP-BETA (POTENTIAL).
 FT CHAIN 672 770 C99 (POTENTIAL).
 FT CHAIN 672 713 BETA-AMYLOID PROTEIN 42 (POTENTIAL).
 FT CHAIN 672 711 BETA-AMYLOID PROTEIN 40 (POTENTIAL).
 FT CHAIN 688 770 C83 (POTENTIAL).
 FT CHAIN 688 713 P3(42) (POTENTIAL).

FT	CHAIN	688	711	P3(40) (POTENTIAL).
FT	CHAIN	712	770	GAMMA-CTF(59) (POTENTIAL).
FT	CHAIN	714	770	GAMMA-CTF(57) (POTENTIAL).
FT	CHAIN	721	770	GAMMA-CTF(50) (POTENTIAL).
FT	CHAIN	740	770	C31 (POTENTIAL).
FT	DOMAIN	18	699	EXTRACELLULAR (POTENTIAL).
FT	TRANSMEM	700	723	POTENTIAL.
FT	DOMAIN	724	770	CYTOPLASMIC (POTENTIAL).
FT	DOMAIN	96	110	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	181	188	ZINC-BINDING (BY SIMILARITY).
FT	DOMAIN	291	341	BPTI/KUNITZ INHIBITOR.
FT	DOMAIN	391	423	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	491	522	HEPARIN-BINDING (BY SIMILARITY).
FT	DOMAIN	523	540	COLLAGEN-BINDING (BY SIMILARITY).
FT	DOMAIN	732	751	INTERACTION WITH G(O)-ALPHA
FT				(BY SIMILARITY).
FT	DOMAIN	230	260	ASP/GLU-RICH (ACIDIC).
FT	DOMAIN	274	280	POLY-THR.
FT	SITE	144	144	REQUIRED FOR COPPER(II) REDUCTION
FT				(BY SIMILARITY).
FT	ACT_SITE	301	302	REACTIVE BOND (BY SIMILARITY).
FT	SITE	671	672	CLEAVAGE (BY BETA-SECRETASE)
FT				(BY SIMILARITY).
FT	SITE	672	673	CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
FT	SITE	687	688	CLEAVAGE (BY ALPHA-SECRETASE)
FT				(BY SIMILARITY).
FT	SITE	704	704	IMPLICATED IN FREE RADICAL PROPAGATION
FT				(BY SIMILARITY).
FT	SITE	706	706	INVOLVED IN OXIDATIVE REACTIONS
FT				(BY SIMILARITY).
FT	SITE	711	712	CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT				(BY SIMILARITY).
FT	SITE	713	714	CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT				(BY SIMILARITY).
FT	SITE	720	721	CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)
FT				(BY SIMILARITY).
FT	SITE	724	734	BASOLATERAL SORTING SIGNAL
FT				(BY SIMILARITY).
FT	SITE	739	740	CLEAVAGE (BY CASPASES-3,-6,-8 OR -9)

Query Match 98.1%; Score 3582.5; DB 1; Length 770;
 Best Local Similarity 89.9%; Pred. No. 1.8e-168;
 Matches 692; Conservative 2; Mismatches 1; Indels 75; Gaps 1;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240

Db	181	 GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
Qy	241	EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVR-----	288
Db	241	 EADDDDEDDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVREVCSEAETGPC	300
Qy	289	-----	288
Db	301	RAMISRWFVDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSVMSQSLRKTTREPLTRD	360
Qy	289	---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA	345
Db	361	: PVKLPPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA	420
Qy	346	KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL	405
Db	421	 KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL	480
Qy	406	QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	465
Db	481	 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	540
Qy	466	MNQSLSLLYNVPAAVEEQDEVDLLQKEQNYSDVLANMISEPRISYGNDALMPSLTET	525
Db	541	 MNQSLSLLYNVPAAVEEQDEVDLLQKEQNYSDVLANMISEPRISYGNDALMPSLTET	600
Qy	526	KTTVELLPVNGEFSDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN	585
Db	601	 KTTVELLPVNGEFSDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN	660
Qy	586	IKTEEISEVNLDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL	645
Db	661	: IKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL	720
Qy	646	VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQQMN	695
Db	721	 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQQMN	770

RESULT 3

A4_SAISC

ID	A4_SAISC	STANDARD;	PRT;	751 AA.
AC	Q95241;			
DT	15-DEC-1998 (Rel. 37, Created)			
DT	15-DEC-1998 (Rel. 37, Last sequence update)			
DT	10-OCT-2003 (Rel. 42, Last annotation update)			
DE	Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid			
DE	protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha); Soluble			
DE	APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-APP42);			
DE	Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40); Gamma-			
DE	CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)			
DE	(Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-			
DE	secretase C-terminal fragment 50); C31].			
GN	APP.			
OS	Saimiri sciureus (Common squirrel monkey).			
OC	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;			

OC Mammalia; Eutheria; Primates; Platyrrhini; Cebidae; Cebinae; Saimiri.
 OX NCBI_TaxID=9521;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC TISSUE=Kidney, and Liver;
 RX MEDLINE=96108492; PubMed=8532114;
 RA Levy E., Amorim A., Frangione B., Walker L.C.;
 RT "Beta-amyloid precursor protein gene in squirrel monkeys with
 RT cerebral amyloid angiopathy.";
 RL Neurobiol. Aging 16:805-808(1995).
 CC -!- FUNCTION: Functions as a cell surface receptor and performs
 CC physiological functions on the surface of neurons relevant to
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in
 CC cell mobility and transcription regulation through protein-protein
 CC interactions (By similarity). Can promote transcription activation
 CC through binding to APBB1/Tip60 and inhibit Notch signaling through
 CC interaction with Numb (By similarity). Couples to apoptosis-
 CC inducing pathways such as those mediated by G(0) and JIP (By
 CC similarity). Inhibits G(0) alpha ATPase activity (By similarity).
 CC Acts as a kinesin I membrane receptor, mediating the axonal
 CC transport of beta-secretase and presenilin 1 (By similarity). May
 CC be involved in copper homeostasis/oxidative stress through copper
 CC ion reduction. In vitro, copper-metallated APP induces neuronal
 CC death directly or is potentiated through Cu(II)-mediated low-
 CC density lipoprotein oxidation (By similarity). Can regulate
 CC neurite outgrowth through binding to components of the
 CC extracellular matrix such as heparin and collagen I and IV (By
 CC similarity). The splice isoforms that contain the BPTI domain
 CC possess protease inhibitor activity (By similarity).
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
 CC with metal-reducing activity. Bind transient metals such as
 CC copper, zinc and iron (By similarity).
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
 CC peptides, including C31, are potent enhancers of neuronal
 CC apoptosis (By similarity).
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
 CC cytoplasmic proteins, including APBB family members, the APBA
 CC family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding
 CC to Dab1 inhibits its serine phosphorylation (By similarity). Also
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
 CC (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.
 CC In vitro, it binds MAPT via the MT-binding domains (By
 CC similarity). Associates with microtubules in the presence of ATP
 CC and in a kinesin-dependent manner (By similarity).
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
 CC protein that rapidly becomes internalized via clathrin-coated
 CC pits. During maturation, the immature APP (N-glycosylated in the
 CC endoplasmic reticulum) moves to the Golgi complex where complete
 CC maturation occurs (O-glycosylated and sulfated). After alpha-
 CC secretase cleavage, soluble APP is released into the extracellular
 CC space and the C-terminal is internalized to endosomes and
 CC lysosomes. Some APP accumulates in secretory transport vesicles
 CC leaving the late Golgi compartment and returns to the cell
 CC surface. Gamma-CTF(59) peptide is located to both the cytoplasm
 CC and nuclei of neurons (By similarity).
 CC -!- ALTERNATIVE PRODUCTS:
 CC Event=Alternative splicing; Named isoforms=2;

CC Comment=Additional isoforms seem to exist;
 CC Name=APP770;
 CC IsoId=Q95241-1; Sequence=Displayed;
 CC Name=APP695;
 CC IsoId=Q95241-2; Sequence=Not described;
 CC -!- DOMAIN: The basolateral sorting signal (BaSS) is required for
 CC sorting of membrane proteins to the basolateral surface of
 CC epithelial cells (By similarity).
 CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
 CC phosphorylated proteins is required for the specific binding of
 CC the PID domain. However additional amino acids either N- or C-
 CC terminal to the NPXY motif are often required for complete
 CC interaction. The PID domain-containing proteins which bind APP
 CC require the YENPTY motif for full interaction. These interactions
 CC are independent of phosphorylation on the terminal tyrosine
 CC residue. The NPXY site is also involved in clathrin-mediated
 CC endocytosis (By similarity).
 CC -!- PTM: Proteolytically processed under normal cellular conditions.
 CC Cleavage by alpha-secretase or alternatively by beta-secretase
 CC leads to generation and extracellular release of soluble APP
 CC peptides, S-APP-alpha and S-APP-beta, respectively, and the
 CC retention of corresponding membrane-anchored C-terminal fragments,
 CC C83 and C99. Subsequent processing of C83 by gamma-secretase
 CC yields P3 peptides. This is the major secretory pathway and is
 CC nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated
 CC gamma-secretase processing of C99 releases the amyloid beta
 CC proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),
 CC major components of amyloid plaques, and the cytotoxic C-terminal
 CC fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By
 CC similarity).
 CC -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis.
 CC (By similarity). Cleavage at Asp-720 by either caspase-3, -8 or -9
 CC results in the production of the neurotoxic C31 peptide and the
 CC increased production of beta-amyloid peptides (By similarity).
 CC -!- PTM: N- and O-glycosylated (By similarity).
 CC -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
 CC serine residues is neuron-specific. Phosphorylation can affect APP
 CC processing, neuronal differentiation and interaction with other
 CC proteins (By similarity).
 CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
 CC zinc, can induce histidine-bridging between beta-amyloid molecules
 CC resulting in beta-amyloid-metal aggregates (By similarity).
 CC Extracellular zinc-binding increases binding of heparin to APP and
 CC inhibits collagen-binding (By similarity).
 CC -!- SIMILARITY: Belongs to the APP family.
 CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
 CC -----
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
 CC the European Bioinformatics Institute. There are no restrictions on its
 CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by and for commercial
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
 CC or send an email to license@isb-sib.ch).
 CC -----
 CC DR EMBL; S81024; AAD14347.1; -.
 CC DR HSSP; P05067; 1AAP.

DR InterPro; IPR008155; A4_APP.
 DR InterPro; IPR008154; A4_extra.
 DR InterPro; IPR001255; Beta-APP.
 DR InterPro; IPR002223; Kunitz_BPTI.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR Pfam; PF03494; Beta-APP; 1.
 DR Pfam; PF00014; Kunitz_BPTI; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR PRINTS; PR00759; BASICPTASE.
 DR ProDom; PD000222; Kunitz_BPTI; 1.
 DR SMART; SM00006; A4_EXTRA; 1.
 DR SMART; SM00131; KU; 1.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 DR PROSITE; PS00280; BPTI_KUNITZ_1; 1.
 DR PROSITE; PS50279; BPTI_KUNITZ_2; 1.
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
 KW Proteoglycan; Amyloid; Alternative splicing.
 FT SIGNAL 1 17 BY SIMILARITY.
 FT CHAIN 18 751 A4 PROTEIN.
 FT CHAIN 18 668 SOLUBLE APP-ALPHA (POTENTIAL).
 FT CHAIN 18 652 SOLUBLE APP-BETA (POTENTIAL).
 FT CHAIN 653 751 C99 (POTENTIAL).
 FT CHAIN 653 694 BETA-AMYLOID PROTEIN 42 (POTENTIAL).
 FT CHAIN 653 692 BETA-AMYLOID PROTEIN 40 (POTENTIAL).
 FT CHAIN 669 751 C83 (POTENTIAL).
 FT CHAIN 669 694 P3(42) (POTENTIAL).
 FT CHAIN 669 692 P3(40) (POTENTIAL).
 FT CHAIN 693 751 GAMMA-CTF(59) (POTENTIAL).
 FT CHAIN 695 751 GAMMA-CTF(57) (POTENTIAL).
 FT CHAIN 702 751 GAMMA-CTF(50) (POTENTIAL).
 FT CHAIN 721 751 C31 (POTENTIAL).
 FT DOMAIN 18 680 EXTRACELLULAR (POTENTIAL).
 FT TRANSMEM 681 704 POTENTIAL.
 FT DOMAIN 705 751 CYTOPLASMIC (POTENTIAL).
 FT DOMAIN 96 110 HEPARIN-BINDING (BY SIMILARITY).
 FT DOMAIN 181 188 ZINC-BINDING (BY SIMILARITY).
 FT DOMAIN 291 341 BPTI/KUNITZ INHIBITOR.
 FT DOMAIN 316 344 HEPARIN-BINDING (BY SIMILARITY).
 FT DOMAIN 363 428 HEPARIN-BINDING (BY SIMILARITY).
 FT DOMAIN 504 521 COLLAGEN-BINDING (BY SIMILARITY).
 FT DOMAIN 713 732 INTERACTION WITH G(O)-ALPHA
 FT (BY SIMILARITY).
 FT DOMAIN 230 260 ASP/GLU-RICH (ACIDIC).
 FT DOMAIN 274 280 POLY-THR.
 FT SITE 144 144 REQUIRED FOR COPPER(II) REDUCTION
 FT (BY SIMILARITY).
 FT ACT_SITE 301 302 REACTIVE BOND.
 FT SITE 652 653 CLEAVAGE (BY BETA-SECRETASE)
 FT (BY SIMILARITY).
 FT SITE 653 654 CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
 FT SITE 668 669 CLEAVAGE (BY ALPHA-SECRETASE)
 FT (BY SIMILARITY).
 FT SITE 685 685 INVOLVED IN FREE RADICAL PROPAGATION
 FT (BY SIMILARITY).

FT	SITE	687	687	INVOLVED IN OXIDATIVE REACTIONS
FT				(BY SIMILARITY).
FT	SITE	692	693	CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT				(BY SIMILARITY).
FT	SITE	694	695	CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT				(BY SIMILARITY).
FT	SITE	701	702	CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)
FT				(BY SIMILARITY).
FT	SITE	705	715	BASOLATERAL SORTING SIGNAL
FT				(BY SIMILARITY).
FT	SITE	720	721	CLEAVAGE (BY CASPASES-3,-6,-8 OR -9)
FT				(BY SIMILARITY).
FT	SITE	738	741	ENDOCYTOSIS SIGNAL.
FT	SITE	740	743	NPXY MOTIF.

Query Match 97.9%; Score 3576; DB 1; Length 751;
 Best Local Similarity 91.7%; Pred. No. 3.6e-168;
 Matches 689; Conservative 3; Mismatches 3; Indels 56; Gaps 1;

Qy	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Db	1	MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK	60
Qy	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG	120
Db	61	TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRDRKQCKTHPHIVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
		:	
Db	181	GVEFVCCPLAEESDHVDSADAEEDSDVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE	240
Qy	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVR-----	288
Db	241	EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTESVEEVVREVCSEAETGPC	300
Qy	289	-----VPTTAASTPDAVDKYL	304
		:	
Db	301	RAMISRWFVDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSVIPTTAASTPDAVDKYL	360
Qy	305	ETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQEKV	364
Db	361	ETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPKADKKAVIQHFQEKV	420
Qy	365	ESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVR	424
Db	421	ESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVR	480
Qy	425	AEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQ	484
Db	481	AEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAAVEEIQ	540
Qy	485	DEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSLDDLQ	544

```

Db      541 DEVDELLQKEQNYSDVLNMISEPRISYGNDAIMPSTETKTTVELLPVNGEFSLLDLQ 600
Qy      545 PWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEI SEVNLD AEF RHDS 604
        |||
Db      601 PWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTNIKTEEI SEVKMD AEF RHDS 660
Qy      605 GYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSI HHGVVEVD 664
        |||
Db      661 GYEVHHQKL VFFAEDVGSNKGAI IGLMVGGVVIATVIVITLVMLKKKQYTSI HHGVVEVD 720
Qy      665 AAVTPEERHLSKMQQNGYENPTYKFFE QMQN 695
        |||
Db      721 AAVTPEERHLSKMQQNGYENPTYKFFE QMQN 751

```

RESULT 4

A4_PIG

```

ID      A4_PIG          STANDARD;          PRT;      770 AA.
AC      P79307; Q29023; Q9TUI0;
DT      01-NOV-1997 (Rel. 35, Created)
DT      10-OCT-2003 (Rel. 42, Last sequence update)
DT      10-OCT-2003 (Rel. 42, Last annotation update)
DE      Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE      amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE      Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-
DE      APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);
DE      Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE      (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE      secretase C-terminal fragment 50); C31].
OS      Sus scrofa (Pig).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Mammalia; Eutheria; Cetartiodactyla; Suina; Suidae; Sus.
OX      NCBI_TaxID=9823;
RN      [1]
RP      SEQUENCE FROM N.A.
RA      Kimura A., Takahashi T.;
RT      "Amyloid precursor protein 770.";
RL      Submitted (SEP-1999) to the EMBL/GenBank/DDBJ databases.
RN      [2]
RP      SEQUENCE OF 1-136 FROM N.A.
RC      TISSUE=Small intestine;
RA      Winteroe A.K., Fredholm M.;
RT      "Evaluation and characterization of a porcine small intestine cDNA
RT      library.";
RL      Submitted (JAN-1997) to the EMBL/GenBank/DDBJ databases.
RN      [3]
RP      SEQUENCE OF 667-723 FROM N.A.
RC      TISSUE=Brain;
RX      MEDLINE=92017079; PubMed=1656157;
RA      Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT      "Conservation of the sequence of the Alzheimer's disease amyloid
RT      peptide in dog, polar bear and five other mammals by cross-species
RT      polymerase chain reaction analysis.";
RL      Brain Res. Mol. Brain Res. 10:299-305(1991).
CC      -!- FUNCTION: Functions as a cell surface receptor and performs
CC      physiological functions on the surface of neurons relevant to
CC      neurite growth, neuronal adhesion and axonogenesis. Involved in

```

cell mobility and transcription regulation through protein-protein interactions (By similarity). Can promote transcription activation through binding to APBB1/Tip60 and inhibit Notch signaling through interaction with Numb (By similarity). Couples to apoptosis-inducing pathways such as those mediated by G(O) and JIP (By similarity). Inhibits G(O) alpha ATPase activity (By similarity). Acts as a kinesin I membrane receptor, mediating the axonal transport of beta-secretase and presenilin 1 (By similarity). May be involved in copper homeostasis/oxidative stress through copper ion reduction (By similarity). In vitro, copper-metallated APP induces neuronal death directly or is potentiated through Cu(II)-mediated low-density lipoprotein oxidation (By similarity). Can regulate neurite outgrowth through binding to components of the extracellular matrix such as heparin and collagen I and IV (By similarity).

-!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators with metal-reducing activity. Bind transient metals such as copper, zinc and iron (By similarity).

-!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved peptides, including C31, are potent enhancers of neuronal apoptosis (By similarity).

-!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several cytoplasmic proteins, including APBB family members, the APBA family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding to Dab1 inhibits its serine phosphorylation (By similarity). Also interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2 (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1. In vitro, it binds MAPT via the MT-binding domains (By similarity). Associates with microtubules in the presence of ATP and in a kinesin-dependent manner (By similarity).

-!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface protein that rapidly becomes internalized via clathrin-coated pits. During maturation, the immature APP (N-glycosylated in the endoplasmic reticulum) moves to the Golgi complex where complete maturation occurs (O-glycosylated and sulfated). After alpha-secretase cleavage, soluble APP is released into the extracellular space and the C-terminal is internalized to endosomes and lysosomes. Some APP accumulates in secretory transport vesicles leaving the late Golgi compartment and returns to the cell surface. Gamma-CTF(59) peptide is located to both the cytoplasm and nuclei of neurons (By similarity).

-!- DOMAIN: The basolateral sorting signal (BaSS) is required for sorting of membrane proteins to the basolateral surface of epithelial cells (By similarity).

-!- DOMAIN: The NPXY sequence motif found in many tyrosine-phosphorylated proteins is required for the specific binding of the PID domain. However additional amino acids either N- or C-terminal to the NPXY motif are often required for complete interaction. The PID domain-containing proteins which bind APP require the YENPTY motif for full interaction. These interactions are independent of phosphorylation on the terminal tyrosine residue. The NPXY site is also involved in clathrin-mediated endocytosis (By similarity).

-!- PTM: Proteolytically processed under normal cellular conditions. Cleavage by alpha-secretase or alternatively by beta-secretase leads to generation and extracellular release of soluble APP peptides, S-APP-alpha and S-APP-beta, respectively, and the

CC retention of corresponding membrane-anchored C-terminal fragments,
 CC C83 and C99. Subsequent processing of C83 by gamma-secretase
 CC yields P3 peptides. This is the major secretory pathway and is
 CC nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated
 CC gamma-secretase processing of C99 releases the amyloid beta
 CC proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),
 CC major components of amyloid plaques, and the cytotoxic C-terminal
 CC fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By
 CC similarity).
 CC -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis
 CC (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9
 CC results in the production of the neurotoxic C31 peptide and the
 CC increased production of beta-amyloid peptides (By similarity).
 CC -!- PTM: N- and O-glycosylated (By similarity).
 CC -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
 CC serine residues is neuron-specific. Phosphorylation can affect APP
 CC processing, neuronal differentiation and interaction with other
 CC proteins (By similarity).
 CC -!- PTM: Extracellular binding and reduction of copper, results in a
 CC corresponding oxidation of Cys-144 and Cys-158, and the formation
 CC of a disulfide bond (By similarity).
 CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
 CC zinc, can induce histidine-bridging between beta-amyloid molecules
 CC resulting in beta-amyloid-metal aggregates (By similarity).
 CC Extracellular zinc-binding increases binding of heparin to APP and
 CC inhibits collagen-binding (By similarity).
 CC -!- SIMILARITY: Belongs to the APP family.
 CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

CC -----
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
 CC the European Bioinformatics Institute. There are no restrictions on its
 CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by and for commercial
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
 CC or send an email to license@isb-sib.ch).
 CC -----

DR EMBL; AB032550; BAA84580.1; -.
 DR EMBL; Z84022; CAB06313.1; -.
 DR EMBL; X56127; CAA39592.1; -.
 DR HSSP; P05067; 1AAP.
 DR InterPro; IPR008155; A4_APP.
 DR InterPro; IPR008154; A4_extra.
 DR InterPro; IPR002223; Kunitz_BPTI.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR PRINTS; PR00759; BASICPTASE.
 DR ProDom; PD000222; Kunitz_BPTI; 1.
 DR SMART; SM00006; A4_EXTRA; 1.
 DR SMART; SM00131; KU; 1.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 DR PROSITE; PS00280; BPTI_KUNITZ_1; 1.
 DR PROSITE; PS50279; BPTI_KUNITZ_2; 1.
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;

Db	61	TCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRSRKQCKTHTHIVIPYRCLVG	120
Qy	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Db	121	EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR	180
Qy	181	GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEE	240
		:	
Db	181	GVEFVCCPLAEESDNIDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVADVEEE	240
Qy	241	EADDDDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTSVEEVVR-----	288
		:	
Db	241	EAEDDEDDEDGDEVEEEAEEPYEEATERTTSIATTTTTTTSVEEVVREVCSEQAETGPC	300
Qy	289	-----	288
Db	301	RAMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSVMSQSLLKTTQEHLPOD	360
Qy	289	---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA	345
		:	
Db	361	PVKLPPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA	420
Qy	346	KNLPKADKKAVIQHFQEKVESLEQEAAERQQLVETHMARVEAMLNDRRLALENYITAL	405
Db	421	KNLPKADKKAVIQHFQEKVESLEQEAAERQQLVETHMARVEAMLNDRRLALENYITAL	480
Qy	406	QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	465
Db	481	QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER	540
Qy	466	MNQSLSLLYNVPAAVEEIQDEVDLLQKEQNYSDVLNMISEPRISYGNDALMPSLTET	525
Db	541	MNQSLSLLYNVPAAVEEIQDEVDLLQKEQNYSDVLNMISEPRISYGNDALMPSLTET	600
Qy	526	KTTVELLPVNGEFSDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPGSGLTN	585
Db	601	KTTVELLPVNGEFSDDLQPWHPFGVDSVPANTENEVEPVDARPAADRGLTTRPGSGLTN	660
Qy	586	IKTEEISEVNLDAEFRHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITL	645
		:	
Db	661	IKTEEISEVKMDAEFRHDSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITL	720
Qy	646	VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQQMN	695
Db	721	VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQQMN	770

RESULT 5

A4_CAVPO

ID A4_CAVPO STANDARD; PRT; 770 AA.

AC Q60495; Q60496;

DT 10-OCT-2003 (Rel. 42, Created)

DT 10-OCT-2003 (Rel. 42, Last sequence update)

DT 10-OCT-2003 (Rel. 42, Last annotation update)

DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease

DE amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);

DE Soluble APP-beta (S-APP-beta); CTF-alpha; CTF-beta; Beta-amyloid

DE protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); P3(42);
DE P3(40); CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-
DE CTF(57) (Gamma-secretase C-terminal fragment 57); C31].
GN APP.
OS Cavia porcellus (Guinea pig).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Hystricognathi; Caviidae; Cavia.
OX NCBI_TaxID=10141;
RN [1]
RP SEQUENCE FROM N.A., AND ALTERNATIVE SPLICING.
RC TISSUE=Brain, and Liver;
RX MEDLINE=97236426; PubMed=9116031;
RA Beck M., Mueller D., Bigl V.;
RT "Amyloid precursor protein in Guinea pigs - complete cDNA sequence and
RT alternative splicing."
RL Biochim. Biophys. Acta 1351:17-21(1997).
RN [2]
RP INTERACTION OF BETA-APP40 WITH APOE.
RX MEDLINE=98007700; PubMed=9349544;
RA Martel C.L., Mackic J.B., Matsubara E., Governale S., Miguel C.,
RA Miao W., McComb J.G., Frangione B., Ghiso J., Zlokovic B.V.;
RT "Isoform-specific effects of apolipoproteins E2, E3, and E4 on
RT cerebral capillary sequestration and blood-brain barrier transport of
RT circulating Alzheimer's amyloid beta."
RL J. Neurochem. 69:1995-2004(1997).
RN [3]
RP PROCESSING.
RX MEDLINE=20084499; PubMed=10619481;
RA Beck M., Brueckner M.K., Holzer M., Kaap S., Pannicke T., Arendt T.,
RA Bigl V.;
RT "Guinea-pig primary cell cultures provide a model to study expression
RT and amyloidogenic processing of endogenous amyloid precursor
RT protein."
RL Neuroscience 95:243-254(2000).
RN [4]
RP GAMMA-SECRETASE PROCESSING.
RX MEDLINE=20576391; PubMed=11035007;
RA Pinnix I., Musunuru U., Tun H., Sridharan A., Golde T., Eckman C.,
RA Ziani-Cherif C., Onstead L., Sambamurti K.;
RT "A novel gamma -secretase assay based on detection of the putative
RT C-terminal fragment-gamma of amyloid beta protein precursor."
RL J. Biol. Chem. 276:481-487(2001).
CC -!- FUNCTION: Functions as a cell surface receptor and performs
CC physiological functions on the surface of neurons relevant to
CC neurite growth, neuronal adhesion and axonogenesis. Involved in
CC cell mobility and transcription regulation through protein-protein
CC interactions (By similarity). Can promote transcription activation
CC through binding to APBB1/Tip60 and inhibit Notch signaling through
CC interaction with Numb (By similarity). Couples to apoptosis-
CC inducing pathways such as those mediated by G(O) and JIP (By
CC similarity). Inhibits G(O) alpha ATPase activity (By similarity).
CC Acts as a kinesin I membrane receptor, mediating the axonal
CC transport of beta-secretase and presenilin 1 (By similarity). May
CC be involved in copper homeostasis/oxidative stress through copper
CC ion reduction (By similarity). In vitro, copper-metallated APP
CC induces neuronal death directly or is potentiated through Cu(II)-
CC mediated low-density lipoprotein oxidation (By similarity). Can

CC regulate neurite outgrowth through binding to components of the
 CC extracellular matrix such as heparin and collagen I and IV (By
 CC similarity). The splice isoforms that contain the BPTI domain
 CC possess protease inhibitor activity (By similarity).
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
 CC with metal-reducing activity. Bind transient metals such as
 CC copper, zinc and iron. Beta-amyloid peptides bind to lipoproteins
 CC and apolipoproteins E and J in the CSF and to HDL particles in
 CC plasma, inhibiting metal-catalyzed oxidation of lipoproteins.
 CC -!- FUNCTION: Appicans elicit adhesion of neural cells to the
 CC extracellular matrix and may regulate neurite outgrowth in the
 CC brain (By similarity).
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
 CC peptides, including C31, are potent enhancers of neuronal
 CC apoptosis (By similarity).
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
 CC cytoplasmic proteins, including APBB family members, the APBA
 CC family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Also
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
 CC (via its TPR domains), APPBP2 (via BaSS) and DDB1 (By similarity).
 CC Associates with microtubules in the presence of ATP and in a
 CC kinesin-dependent manner (By similarity). Soluble Abeta40 binds
 CC all three isoforms of APOE, in vitro and in vivo. When lipidated,
 CC ApoE3 appears to be the preferred amyloid binding isoform, while
 CC the apoE4 isoform-beta-APP40 complex is capable of being
 CC transported across the blood-brain barrier.
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
 CC protein that rapidly becomes internalized via clathrin-coated pits
 CC (By similarity). During maturation, the immature APP (N-
 CC glycosylated in the endoplasmic reticulum) moves to the Golgi
 CC complex where complete maturation occurs (O-glycosylated and
 CC sulfated) (By similarity). After alpha-secretase cleavage, soluble
 CC APP is released into the extracellular space and the C-terminal is
 CC internalized to endosomes and lysosomes (By similarity). Some APP
 CC accumulates in secretory transport vesicles leaving the late Golgi
 CC compartment and returns to the cell surface (By similarity). APP
 CC sorts to the basolateral surface in epithelial cells (By
 CC similatity).
 CC -!- ALTERNATIVE PRODUCTS:
 CC Event=Alternative splicing; Named isoforms=2;
 CC Comment=Additional isoforms, missing exons 7,8 and 15, seem to
 CC exist. The L-isoforms, missing exon 15, are referred to as
 CC appicans;
 CC Name=APP770;
 CC IsoId=Q60495-1; Sequence=Displayed;
 CC Name=APP695;
 CC IsoId=Q60495-2; Sequence=VSP_007221, VSP_007222;
 CC -!- TISSUE SPECIFICITY: Isoform APP695 is the major isoform found in
 CC brain. The longer isoforms containing the BPTI domain are
 CC predominantly expressed in peripheral organs such as muscle and
 CC liver.
 CC -!- INDUCTION: Increased levels during neuronal differentiation.
 CC -!- DOMAIN: The basolateral sorting signal (BaSS) is required for
 CC sorting of membrane proteins to the basolateral surface of
 CC epithelial cells.
 CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
 CC phosphorylated proteins is required for the specific binding of

CC the PID domain. However additional amino acids either N- or C-
 CC terminal to the NPXY motif are often required for complete
 CC interaction. The PID domain-containing proteins which bind APP
 CC require the YENPTY motif for full interaction. These interactions
 CC are independent of phosphorylation on the terminal tyrosine
 CC residue (By similarity). The NPXY site is also involved in
 CC clathrin-mediated endocytosis.

- CC -!- PTM: Proteolytically processed under normal cellular conditions.
 CC Cleavage by alpha-secretase or alternatively by beta-secretase
 CC leads to generation and extracellular release of soluble APP
 CC peptides, S-APP-alpha and S-APP-beta, respectively, and the
 CC retention of corresponding membrane-anchored C-terminal fragments,
 CC CTF-alpha and CTF-beta. Subsequent processing of CTF-alpha by
 CC gamma-secretase yields P3 peptides. This is the major secretory
 CC pathway and is nonamyloidogenic. Alternatively,
 CC presenilin/nicastrin-mediated gamma-secretase processing of CTF-
 CC beta releases the amyloid beta proteins, amyloid-beta 40 (Abeta40)
 CC and amyloid-beta 42 (Abeta42), major components of amyloid
 CC plaques, and the corresponding cytotoxic C-terminal fragments
 CC (CTFs).
- CC -!- PTM: Proteolytically cleaved by caspase-3 during neuronal
 CC apoptosis (By similarity).
- CC -!- PTM: N- and O-glycosylated. O-linkage of chondroitin sulfate to
 CC the L-APP isoforms produces the APP proteoglycan core proteins,
 CC the appicans (By similarity).
- CC -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
 CC serine residues is neuron-specific (By similarity).
 CC Phosphorylation can affect APP processing, neuronal
 CC differentiation and interaction with other proteins.
- CC -!- PTM: Extracellular binding and reduction of copper, results in a
 CC corresponding oxidation of Cys-144 and Cys-158, and the formation
 CC of a disulfide bond (By similarity).
- CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
 CC zinc, can induce histidine-bridging between beta-amyloid molecules
 CC resulting in beta-amyloid-metal aggregates.
- CC -!- SIMILARITY: Belongs to the APP family.
- CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

CC -----
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
 CC the European Bioinformatics Institute. There are no restrictions on its
 CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by and for commercial
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
 CC or send an email to license@isb-sib.ch).
 CC -----

DR EMBL; X97631; CAA66230.1; -.
 DR EMBL; X99198; CAA67589.1; -.
 DR HSSP; P05067; 1BA4.
 DR InterPro; IPR008155; A4_APP.
 DR InterPro; IPR008154; A4_extra.
 DR InterPro; IPR002223; Kunitz_BPTI.
 DR Pfam; PF00014; Kunitz_BPTI; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR PRINTS; PR00759; BASICPTASE.
 DR ProDom; PD000222; Kunitz_BPTI; 1.
 DR SMART; SM00006; A4_EXTRA; 1.

DR SMART; SM00131; KU; 1.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 DR PROSITE; PS00280; BPTI_KUNITZ_1; 1.
 DR PROSITE; PS50279; BPTI_KUNITZ_2; 1.
 KW Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
 KW Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
 KW Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
 KW Proteoglycan; Alternative splicing; Amyloid.
 FT SIGNAL 1 17 BY SIMILARITY.
 FT CHAIN 18 770 AMYLOID BETA A4 PROTEIN.
 FT CHAIN 18 687 SOLUBLE APP-ALPHA (BY SIMILARITY).
 FT CHAIN 18 671 SOLUBLE APP-BETA (BY SIMILARITY).
 FT CHAIN 672 770 CTF-ALPHA (BY SIMILARITY).
 FT CHAIN 672 713 BETA-AMYLOID PROTEIN 42 (BY SIMILARITY).
 FT CHAIN 672 711 BETA-AMYLOID PROTEIN 40 (BY SIMILARITY).
 FT CHAIN 688 770 CTF-BETA (BY SIMILARITY).
 FT CHAIN 688 713 P3(42) (BY SIMILARITY).
 FT CHAIN 688 711 P3(40) (BY SIMILARITY).
 FT CHAIN 712 770 GAMMA-CTF(59) (BY SIMILARITY).
 FT CHAIN 714 770 GAMMA-CTF(57) (BY SIMILARITY).

Query Match 96.3%; Score 3514.5; DB 1; Length 770;
 Best Local Similarity 87.9%; Pred. No. 3.8e-165;
 Matches 677; Conservative 8; Mismatches 10; Indels 75; Gaps 1;

Qy 1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
 ||| ||||| |||||||||||||||||||||||||:|||||||||: |||||
 Db 1 MLPSLALLLLTTWTARALEVPTDGNAGLLAEPQIAMFCGKLNHMHMNVQNGKWEPPDPSGTK 60
 Qy 61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVPIPYRCLVG 120
 ||| :||||||||||||||||||||||||||||||||||||| |||||||||||||||||
 Db 61 TCIGSKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRSRKQCKTHPHFVPIPYRCLVG 120
 Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
 |||||||||||||||||||||||||||||||||||||||||
 Db 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
 Qy 181 GVEFVCCPLAEESDNVDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
 |||||||||||||||||||||||||||||||||||||:|||||
 Db 181 GVEFVCCPLAEESDNIDSADAEEDDSVWVGADTDYADGSEDKVVEVAEEEEVADVEEEE 240
 Qy 241 EADDDDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTSESVEEVVR----- 288
 ||||| |||||||||||||||||||:|||||||||||||||
 Db 241 EADDDDEDVEDGDEVEEEAEPEYEEATEKTTSIATTTTTTTTSESVEEVVREVCSEQAETGPC 300
 Qy 289 ----- 288
 Db 301 RSMISRWFYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMVCGSVMSQNLLKTSGEVPSQG 360
 Qy 289 ---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA 345
 :|||||||||||||||||||||||||||||||||||||
 Db 361 PVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQA 420
 Qy 346 KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL 405
 |||||||||||||||||||||||||||||||||||||
 Db 421 KNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL 480

Qy 406 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 465
 |||
 Db 481 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 540
 Qy 466 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTET 525
 |||
 Db 541 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMPSLTET 600
 Qy 526 KTTVELLPVNGEFSDDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSGLTN 585
 ||| ||
 Db 601 KTTVELLPVNGEFSDDLQPWHPFGVDSVPANTENEVEPV DARPAADRGLTTRPGSGLTN 660
 Qy 586 IKTEEISEVNLDAEFRHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 645
 ||| : |||
 Db 661 IKTEEISEVKMDAEFRHDSGYEVHHQKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 720
 Qy 646 VMLKKKQYTSIH HGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
 |||
 Db 721 VMLKKKQYTSIH HGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 770

RESULT 6

A4_MOUSE

ID A4_MOUSE STANDARD; PRT; 770 AA.
 AC P12023; P97487; P97942; Q99K32;
 DT 01-OCT-1989 (Rel. 12, Created)
 DT 10-OCT-2003 (Rel. 42, Last sequence update)
 DT 10-OCT-2003 (Rel. 42, Last annotation update)
 DE Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
 DE amyloid protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains:
 DE Soluble APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99
 DE (APP-C99); Beta-amyloid protein 42 (Beta-APP42); Beta-amyloid protein
 DE 40 (Beta-APP40); C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase
 DE C-terminal fragment 59) (Amyloid intracellular domain 59) (AID(59))
 DE (APP-C59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57)
 DE (Amyloid intracellular domain 57) (AID(57)) (APP-C57); Gamma-CTF(50)
 DE (Gamma-secretase C-terminal fragment 50) (Amyloid intracellular domain
 DE 50) (AID(50)); C31].
 GN APP.
 OS Mus musculus (Mouse).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
 OX NCBI_TaxID=10090;
 RN [1]
 RP SEQUENCE FROM N.A. (ISOFORM APP695).
 RC TISSUE=Brain;
 RX MEDLINE=88106489; PubMed=3322280;
 RA Yamada T., Sasaki H., Furuya H., Miyata T., Goto I., Sakaki Y.;
 RT "Complementary DNA for the mouse homolog of the human amyloid beta
 RT protein precursor.";
 RL Biochem. Biophys. Res. Commun. 149:665-671(1987).
 RN [2]
 RP REVISIONS.
 RA Yamada T.;
 RL Submitted (MAR-1988) to the EMBL/GenBank/DDBJ databases.
 RN [3]

RP SEQUENCE FROM N.A. (ISOFORM APP695).
 RC STRAIN=BALB/c; TISSUE=Brain;
 RX MEDLINE=92096458; PubMed=1756177;
 RA de Strooper B., van Leuven F., van den Berghe H.;
 RT "The amyloid beta protein precursor or proteinase nexin II from mouse
 RT is closer related to its human homolog than previously reported.";
 RL Biochim. Biophys. Acta 1129:141-143(1991).
 RN [4]

RP SEQUENCE FROM N.A. (ISOFORM APP695).
 RC STRAIN=SAMP8; TISSUE=Hippocampus;
 RX MEDLINE=21130647; PubMed=11235921;
 RA Kumar V.B., Vyas K., Franko M., Choudhary V., Buddhiraju C.,
 RA Alvarez J., Morley J.E.;
 RT "Molecular cloning, expression, and regulation of hippocampal amyloid
 RT precursor protein of senescence accelerated mouse (SAMP8).";
 RL Biochem. Cell Biol. 79:57-67(2001).
 RN [5]

RP SEQUENCE OF 1-19 FROM N.A.
 RX MEDLINE=92209998; PubMed=1555768;
 RA Izumi R., Yamada T., Yoshikai S.I., Sasaki H., Hattori M.,
 RA Sakai Y.;
 RT "Positive and negative regulatory elements for the expression of the
 RT Alzheimer's disease amyloid precursor-encoding gene in mouse.";
 RL Gene 112:189-195(1992).
 RN [6]

RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP770).
 RC TISSUE=Breast tumor;
 RX MEDLINE=22388257; PubMed=12477932;
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
 RT "Generation and initial analysis of more than 15,000 full-length human
 RT and mouse cDNA sequences.";
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
 RN [7]

RP SEQUENCE OF 281-380 FROM N.A., AND ALTERNATIVE SPLICING.
 RC TISSUE=Brain, and Kidney;
 RX MEDLINE=89149813; PubMed=2493250;
 RA Yamada T., Sasaki H., Dohura K., Goto I., Sakaki Y.;
 RT "Structure and expression of the alternatively-spliced forms of mRNA
 RT for the mouse homolog of Alzheimer's disease amyloid beta protein
 RT precursor.";
 RL Biochem. Biophys. Res. Commun. 158:906-912(1989).

RN [8]
 RP SEQUENCE OF 289-364 FROM N.A.
 RC STRAIN=CD-1; TISSUE=Placenta;
 RX MEDLINE=89345111; PubMed=2569710;
 RA Fukuchi K., Martin G.M., Deeb S.S.;
 RT "Sequence of the protease inhibitor domain of the A4 amyloid protein
 RT precursor of *Mus domesticus*.";
 RL Nucleic Acids Res. 17:5396-5396(1989).
 RN [9]
 RP SEQUENCE OF 656-737 FROM N.A.
 RC STRAIN=129/Sv;
 RA Wragg M.A., Busfield F., Duff K., Korenblat K., Capecchi M.,
 RA Loring J.F., Goate A.M.;
 RT "Introduction of six mutations into the mouse genome using 'Hit and
 RT Run' gene-targeting: introduction of familial Alzheimer's disease
 RT mutations into the mouse amyloid precursor protein gene and
 RT humanization of the A-beta fragment.";
 RL Submitted (DEC-1996) to the EMBL/GenBank/DDBJ databases.
 RN [10]
 RP TISSUE SPECIFICITY OF ALTERNATIVE SPLICED FORMS.
 RX MEDLINE=93287808; PubMed=8510506;
 RA Sola C., Mengod G., Ghetti B., Palacios J.M., Triarhou L.C.;
 RT "Regional distribution of the alternatively spliced isoforms of beta
 RT APP RNA transcript in the brain of normal, heterozygous and
 RT homozygous weaver mutant mice as revealed by in situ hybridization
 RT histochemistry.";
 RL Brain Res. Mol. Brain Res. 17:340-346(1993).
 RN [11]
 RP INTERACTION WITH KNS2.
 RX MEDLINE=21010507; PubMed=11144355;
 RA Kamal A., Stokin G.B., Yang Z., Xia C.-H., Goldstein L.S.;
 RT "Axonal transport of amyloid precursor protein is mediated by direct
 RT binding to the kinesin light chain subunit of kinesin-I.";
 RL Neuron 28:449-459(2000).
 RN [12]
 RP C-TERMINAL PROTEIN-PROTEIN INTERACTIONS, AND MUTAGENESIS OF TYR-728;
 RP THR-743; TYR-757; ASN-759 AND TYR-762.
 RX MEDLINE=21408156; PubMed=11517249;
 RA Matsuda S., Yasukawa T., Homma Y., Ito Y., Niikura T., Hiraki T.,
 RA Hirai S., Ohno S., Kita Y., Kawasumi M., Kouyama K., Yamamoto T.,
 RA Kyriakis J.M., Nishimoto I.;
 RT "C-jun N-terminal kinase (JNK)-interacting protein-1b/islet-brain-1
 RT scaffolds Alzheimer's amyloid precursor protein with JNK.";
 RL J. Neurosci. 21:6597-6607(2001).
 RN [13]
 RP INTERACTION WITH MAPK8IP1, AND PHOSPHORYLATION.
 RX MEDLINE=22028091; PubMed=11912189;
 RA Taru H., Iijima K.-I., Hase M., Kirino Y., Yagi Y., Suzuki T.;
 RT "Interaction of Alzheimer's beta-amyloid precursor family proteins
 RT with scaffold proteins of the JNK signaling cascade.";
 RL J. Biol. Chem. 277:20070-20078(2002).
 RN [14]
 RP INTERACTION OF CTF PEPTIDES WITH NUMB.
 RX MEDLINE=22008109; PubMed=12011466;
 RA Roncarati R., Sestan N., Scheinfeld M.H., Berechid B.E., Lopez P.A.,
 RA Meucci O., McGlade J.C., Rakic P., D'Adamio L.;
 RT "The gamma-secretase-generated intracellular domain of beta-amyloid

RT precursor protein binds Numb and inhibits Notch signaling.";
 RL Proc. Natl. Acad. Sci. U.S.A. 99:7102-7107(2002).
 RN [15]
 RP GAMMA-SECRETASE PROCESSING, AND INTERACTION WITH APBB1.
 RX MEDLINE=21437805; PubMed=11553691;
 RA Cupers P., Orlans I., Craessaerts K., Annaert W., De Strooper B.;
 RT "The amyloid precursor protein (APP)-cytoplasmic fragment generated by
 RT gamma-secretase is rapidly degraded but distributes partially in a
 RT nuclear fraction of neurones in culture.";
 RL J. Neurochem. 78:1168-1178(2001).
 CC -!- FUNCTION: Functions as a cell surface receptor and performs
 CC physiological functions on the surface of neurons relevant to
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in
 CC cell mobility and transcription regulation through protein-protein
 CC interactions. Can promote transcription activation through binding
 CC to APBB1/Tip60 and inhibit Notch signaling through interaction
 CC with Numb. Couples to apoptosis-inducing pathways such as those
 CC mediated by G(O) and JIP. Inhibits G(0) alpha ATPase activity (By
 CC similarity). Acts as a kinesin I membrane receptor, mediating the
 CC axonal transport of beta-secretase and presenilin 1. May be
 CC involved in copper homeostasis/oxidative stress through copper ion
 CC reduction. Can regulate neurite outgrowth through binding to
 CC components of the extracellular matrix such as heparin and
 CC collagen I and IV (By similarity). The splice isoforms that
 CC contain the BPTI domain possess protease inhibitor activity (By
 CC similarity).
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
 CC with metal-reducing activity. Bind transient metals such as
 CC copper, zinc and iron. Rat and mouse beta-amyloid peptides bind
 CC only weakly transient metals and have little reducing activity due
 CC to substitutions of transient metal chelating residues. Beta-APP42
 CC may activate mononuclear phagocytes in the brain and elicit
 CC inflammatory responses. Promotes both tau aggregation and TPK II-
 CC mediated phosphorylation (By similarity).
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
 CC peptides, including C31, are potent enhancers of neuronal
 CC apoptosis.
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
 CC cytoplasmic proteins, including APBB family members, the APBA
 CC family, MAPK8IP1, SHC1, Numb and Dab1. Binding to Dab1 inhibits
 CC its serine phosphorylation. Also interacts with GPCR-like protein
 CC BPP, FPRL1, APPBP1, IB1, KNS2 (via its TPR domains), APPBP2 (via
 CC BaSS) and DDB1 (By similarity). In vitro, it binds MAPT via the
 CC MT-binding domains (By similarity). Associates with microtubules
 CC in the presence of ATP and in a kinesin-dependent manner (By
 CC similarity). Interacts, through a C-terminal domain, with GNAO1
 CC (By similarity). Amyloid beta-42 binds CHRNA7 in hippocampal
 CC neurons (By similarity). Beta-amyloid associates with HADH2 (By
 CC similarity).
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
 CC protein that rapidly becomes internalized via clathrin-coated
 CC pits. During maturation, the immature APP (N-glycosylated in the
 CC endoplasmic reticulum) moves to the Golgi complex where complete

Query Match 95.5%; Score 3485.5; DB 1; Length 770;
 Best Local Similarity 87.5%; Pred. No. 1e-163;
 Matches 674; Conservative 7; Mismatches 14; Indels 75; Gaps 1;

AC P08592;
 DT 01-AUG-1988 (Rel. 08, Created)
 DT 01-DEC-1992 (Rel. 24, Last sequence update)
 DT 10-OCT-2003 (Rel. 42, Last annotation update)
 DE Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid
 DE protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains: Soluble
 DE APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99; Beta-
 DE amyloid protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40);
 DE C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal
 DE fragment 59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57);
 DE Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50); C31].
 GN APP.
 OS Rattus norvegicus (Rat).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
 OX NCBI_TaxID=10116;
 RN [1]
 RP SEQUENCE FROM N.A. (ISOFORM APP695).
 RC TISSUE=Brain;
 RX MEDLINE=88312583; PubMed=2900758;
 RA Shivers B.D., Hilbich C., Multhaup G., Salbaum J.M., Beyreuther K.,
 RA Seeburg P.H.;
 RT "Alzheimer's disease amyloidogenic glycoprotein: expression pattern
 RT in rat brain suggests a role in cell contact.";
 RL EMBO J. 7:1365-1370(1988).
 RN [2]
 RP SEQUENCE OF 289-364 FROM N.A.
 RC TISSUE=Liver;
 RX MEDLINE=89183625; PubMed=2648331;
 RA Kang J., Mueller-Hill B.;
 RT "The sequence of the two extra exons in rat preA4.";
 RL Nucleic Acids Res. 17:2130-2130(1989).
 RN [3]
 RP SEQUENCE OF 720-730, AND MASS SPECTROMETRY.
 RX MEDLINE=21443797; PubMed=11483588;
 RA Gu Y., Misonou H., Sato T., Dohmae N., Takio K., Ihara Y.;
 RT "Distinct intramembrane cleavage of the beta-amyloid precursor protein
 RT family resembling gamma-secretase-like cleavage of Notch.";
 RL J. Biol. Chem. 276:35235-35238(2001).
 RN [4]
 RP ALTERNATIVE SPLICING.
 RX MEDLINE=96187032; PubMed=8624099;
 RA Sandbrink R., Masters C.L., Beyreuther K.;
 RT "APP gene family. Alternative splicing generates functionally related
 RT isoforms.";
 RL Ann. N.Y. Acad. Sci. 777:281-287(1996).
 RN [5]
 RP TISSUE SPECIFICITY OF APPICAN.
 RX MEDLINE=95263526; PubMed=7744833;
 RA Shioi J., Pangalos M.N., Ripellino J.A., Vassilacopoulou D.,
 RA Mytilineou C., Margolis R.U., Robakis N.K.;
 RT "The Alzheimer amyloid precursor proteoglycan (appican) is present in
 RT brain and is produced by astrocytes but not by neurons in primary
 RT neural cultures.";
 RL J. Biol. Chem. 270:11839-11844(1995).
 RN [6]
 RP TISSUE SPECIFICITY OF ISOFORMS.

RX MEDLINE=97150061; PubMed=8996834;
 RA Sandbrink R., Monning U., Masters C.L., Beyreuther K.;
 RT "Expression of the APP gene family in brain cells, brain development
 RT and aging.";
 RL Gerontology 43:119-131(1997).
 RN [7]
 RP INTERACTION WITH DDB1, AND MUTAGENESIS OF TYR-757; ASN-759 AND
 RP TYR-762.
 RX MEDLINE=99127916; PubMed=9930726;
 RA Watanabe T., Sukegawa J., Tomita S., Iijima K.-I., Oguchi S.,
 RA Suzuki T., Nairn A.C., Greengard P.;
 RT "A 127-kDa protein (UV-DDB) binds to the cytoplasmic domain of the
 RT Alzheimer's amyloid precursor protein.";
 RL J. Neurochem. 72:549-556(1999).
 RN [8]
 RP INTERACTION WITH GNAO1, AND MUTAGENESIS OF 732-HIS-HIS-733.
 RX MEDLINE=99162676; PubMed=10024358;
 RA Brouillet E., Trembleau A., Galanaud D., Volovitch M., Bouillot C.,
 RA Valenza C., Prochiantz A., Allinquant B.;
 RT "The amyloid precursor protein interacts with Go heterotrimeric
 RT protein within a cell compartment specialized in signal
 RT transduction.";
 RL J. Neurosci. 19:1717-1727(1999).
 RN [9]
 RP CHARACTERISTICS OF APPICAN, AND MUTAGENESIS OF SER-656.
 RX MEDLINE=95256193; PubMed=7737970;
 RA Pangalos M.N., Efthimiopoulos S., Shioi J., Robakis N.K.;
 RT "The chondroitin sulfate attachment site of appican is formed by
 RT splicing out exon 15 of the amyloid precursor gene.";
 RL J. Biol. Chem. 270:10388-10391(1995).
 RN [10]
 RP BETA-AMYLOID METAL-BINDING.
 RX MEDLINE=99316162; PubMed=10386999;
 RA Huang X., Atwood C.S., Hartshorn M.A., Multhaup G., Goldstein L.E.,
 RA Scarpa R.C., Cuajungco M.P., Gray D.N., Lim J., Moir R.D., Tanzi R.E.,
 RA Bush A.I.;
 RT "The A beta peptide of Alzheimer's disease directly produces hydrogen
 RT peroxide through metal ion reduction.";
 RL Biochemistry 38:7609-7616(1999).
 RN [11]
 RP BETA-AMYLOID ZINC BINDING.
 RX MEDLINE=99343552; PubMed=10413512;
 RA Liu S.T., Howlett G., Barrow C.J.;
 RT "Histidine-13 is a crucial residue in the zinc ion-induced aggregation
 RT of the A beta peptide of Alzheimer's disease.";
 RL Biochemistry 38:9373-9378(1999).
 RN [12]
 RP IMPORTANCE OF GLY-704 IN FREE RADICAL PROPAGATION, AND MUTAGENESIS OF
 RP GLY-704.
 RX MEDLINE=21956095; PubMed=11959460;
 RA Kanski J., Varadarajan S., Aksenova M., Butterfield D.A.;
 RT "Role of glycine-33 and methionine-35 in Alzheimer's amyloid beta-
 RT peptide 1-42-associated oxidative stress and neurotoxicity.";
 RL Biochim. Biophys. Acta 1586:190-198(2001).
 RN [13]
 RP PHOSPHORYLATION.
 RX MEDLINE=97239592; PubMed=9085254;

RA Oishi M., Nairn A.C., Czernik A.J., Lim G.S., Isohara T., Gandy S.E.,
 RA Greengard P., Suzuki T.;
 RT "The cytoplasmic domain of Alzheimer's amyloid precursor protein is
 RT phosphorylated at Thr654, Ser655, and Thr668 in adult rat brain and
 RT cultured cells.";
 RL Mol. Med. 3:111-123(1997).
 RN [14]
 RP PHOSPHORYLATION ON SER-730.
 RX MEDLINE=99262094; PubMed=10329382;
 RA Isohara T., Horiuchi A., Watanabe T., Ando K., Czernik A.J., Uno I.,
 RA Greengard P., Nairn A.C., Suzuki T.;
 RT "Phosphorylation of the cytoplasmic domain of Alzheimer's beta-amyloid
 RT precursor protein at Ser655 by a novel protein kinase.";
 RL Biochem. Biophys. Res. Commun. 258:300-305(1999).
 RN [15]
 RP PHOSPHORYLATION, INDUCTION, SUBCELLULAR LOCATION, AND MUTAGENESIS OF
 RP THR-743.
 RX MEDLINE=99274744; PubMed=10341243;
 RA Ando K., Oishi M., Takeda S., Iijima K.-I., Isohara T., Nairn A.C.,
 RA Kirino Y., Greengard P., Suzuki T.;
 RT "Role of phosphorylation of Alzheimer's amyloid precursor protein
 RT during neuronal differentiation.";
 RL J. Neurosci. 19:4421-4427(1999).
 RN [16]
 RP PHOSPHORYLATION ON THR-743.
 RX MEDLINE=20396183; PubMed=10936190;
 RA Iijima K.-I., Ando K., Takeda S., Satoh Y., Seki T., Itohara S.,
 RA Greengard P., Kirino Y., Nairn A.C., Suzuki T.;
 RT "Neuron-specific phosphorylation of Alzheimer's beta-amyloid precursor
 RT protein by cyclin-dependent kinase 5.";
 RL J. Neurochem. 75:1085-1091(2000).
 RN [17]
 RP CARBOHYDRATE STRUCTURE OF APPICAN.
 RX MEDLINE=21463085; PubMed=11479316;
 RA Tsuchida K., Shioi J., Yamada S., Boghosian G., Wu A., Cai H.,
 RA Sugahara K., Robakis N.K.;
 RT "Appican, the proteoglycan form of the amyloid precursor protein,
 RT contains chondroitin sulfate E in the repeating disaccharide region
 RT and 4-O-sulfated galactose in the linkage region.";
 RL J. Biol. Chem. 276:37155-37160(2001).
 CC -!- FUNCTION: Functions as a cell surface receptor and performs
 CC physiological functions on the surface of neurons relevant to
 CC neurite growth, neuronal adhesion and axonogenesis. Involved in
 CC cell mobility and transcription regulation through protein-protein
 CC interactions (By similarity). Can promote transcription activation
 CC through binding to APBB1/Tip60 and inhibit Notch signaling through
 CC interaction with Numb (By similarity). Couples to apoptosis-
 CC inducing pathways such as those mediated by G(O) and JIP. Inhibits
 CC G(O) alpha ATPase activity. Acts as a kinesin I membrane receptor,
 CC mediating the axonal transport of beta-secretase and presenilin 1
 CC (By similarity). May be involved in copper homeostasis/oxidative
 CC stress through copper ion reduction. Can regulate neurite
 CC outgrowth through binding to components of the extracellular
 CC matrix such as heparin and collagen I and IV (By similarity). The
 CC splice isoforms that contain the BPTI domain possess protease
 CC inhibitor activity (By similarity).
 CC -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators

CC with metal-reducing activity. Bind transient metals such as
 CC copper, zinc and iron. Rat and mouse beta-amyloid peptides bind
 CC only weakly transient metals and have little reducing activity due
 CC to substitutions of transient metal chelating residues. Beta-APP42
 CC may activate mononuclear phagocytes in the brain and elicit
 CC inflammatory responses. Promotes both tau aggregation and TPK II-
 CC mediated phosphorylation (By similarity).
 CC -!- FUNCTION: Appicans elicit adhesion of neural cells to the
 CC extracellular matrix and may regulate neurite outgrowth in the
 CC brain.
 CC -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
 CC peptides, including C31, are potent enhancers of neuronal
 CC apoptosis (By similarity).
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
 CC cytoplasmic proteins, including APBB family members, the APBA
 CC family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Binding
 CC to Dab1 inhibits its serine phosphorylation (By similarity). Also
 CC interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
 CC (via its TPR domains), APPBP2 (via BaSS) (By similarity) and DDB1.
 CC In vitro, it binds MAPT via the MT-binding domains (By
 CC similarity). Associates with microtubules in the presence of ATP
 CC and in a kinesin-dependent manner (By similarity). Interacts,
 CC through a C-terminal domain, with GNAO1. Amyloid beta-42 binds
 CC CHRNA7 in hippocampal neurons (By similarity). Beta-amyloid
 CC associates with HADH2 (By similarity).
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
 CC protein that rapidly becomes internalized via clathrin-coated
 CC pits. During maturation, the immature APP (N-glycosylated in the

Query Match 95.5%; Score 3485.5; DB 1; Length 770;
 Best Local Similarity 87.4%; Pred. No. 1e-163;
 Matches 673; Conservative 9; Mismatches 13; Indels 75; Gaps 1;

```

Qy      1 MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      ||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db      1 MLPSLALLLLAAWTVRALEVPTDGNAGLLAEPQIAMFCGKLNMHMNVQNGKWESDPSGTK 60

Qy     61 TCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      ||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db     61 TCIGTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHTHIVIPYRCLVG 120

Qy    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFR 180

Qy    181 GVEFVCCPLAEESDNVDSADAEEEDSDVWWGGADTDYADGSEDKVVEVAEEEEVAEVEEEE 240
      ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    181 GVEFVCCPLAEESDSIDSADAEEEDSDVWWGGADTDYADGGEDKVVEVAEEEEVADVEEEE 240

Qy    241 EADDDDEDDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVR----- 288
      ||:|||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
Db    241 EAEDDEDVEDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVREVCSEAETGPC 300

Qy    289 ----- 288

Db    301 RAMISRWFVDVTEGKCAPFFYGGCGGNRRNFDTEEYCMVCGSVSSQSLLKTTSEPLPQD 360

```

```

Qy      289 ---VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA 345
      :|||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      361 PVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQA 420

Qy      346 KNLPKADKKAVIQHFQEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITAL 405
      |||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      421 KNLPKADKKAVIQHFQEKVESLEQEAAENERQQLVETHMARVEAMLNDRRLALENYITAL 480

Qy      406 QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 465
      |||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      481 QAVPPRPHHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYER 540

Qy      466 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTET 525
      |||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      541 MNQSLSLLYNVPAAVEEIQDEVDELLQKEQNYSDVLNMISEPRISYGNDALMPSLTET 600

Qy      526 KTTVELLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTN 585
      |||||||||||||||||||| || |||||||||||||||||||||||||||||||
Db      601 KTTVELLPVNGEFSLDDLQPWHPFGVDSVPANTENEVEPVDPARPAADRGLTTRPGSGLTN 660

Qy      586 IKTEEISEVNLDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 645
      |||||||| :|||| ||||:| |||||||||||||||||||||||||||||||
Db      661 IKTEEISEVKMDAEFGHDSGFVHRHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITL 720

Qy      646 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
      |||||||||||||||||||||||||||||||||||||||||||||||||||
Db      721 VMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 770

```

RESULT 8

A4_TETFL

```

ID      A4_TETFL          STANDARD;          PRT;    780 AA.
AC      073683;
DT      10-OCT-2003 (Rel. 42, Created)
DT      10-OCT-2003 (Rel. 42, Last sequence update)
DT      10-OCT-2003 (Rel. 42, Last annotation update)
DE      Alzheimer's disease amyloid A4 protein homolog precursor [Contains:
DE      Beta-amyloid protein (Beta-APP) (A-beta)].
GN      APP.
OS      Tetraodon fluviatilis (Puffer fish).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Actinopterygii; Neopterygii; Teleostei; Euteleostei; Neoteleostei;
OC      Acanthomorpha; Acanthopterygii; Percomorpha; Tetraodontiformes;
OC      Tetraodontoidea; Tetraodontidae; Tetraodon.
OX      NCBI_TaxID=47145;
RN      [1]
RP      SEQUENCE FROM N.A.
RX      MEDLINE=98252138; PubMed=9599080;
RA      Villard L., Tassone F., Crnogorac-Jurcevic T., Clancy K., Gardiner K.;
RT      "Analysis of pufferfish homologues of the AT-rich human APP gene.";
RL      Gene 210:17-24(1998).
CC      !- FUNCTION: Functional neuronal receptor which couples to
CC      intracellular signaling pathway through the GTP-binding protein
CC      G(O) (By similarity).
CC      !- SUBCELLULAR LOCATION: Type I membrane protein.
CC      !- SIMILARITY: Belongs to the APP family.
CC      !- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

```


Db 128 LLVPDKCKFLHQERMNQCESHLHWHTVAKESCGDRAMNLHDYGMLLPCGIDRFRGVEFVC 187

Qy 187 CPLAEESDNVDSADAEEDSDVWVGADTDYADGS-----EDKVVEVAEEE 232
 || || :|| : : ||||| ||:| | ||| ||

Db 188 CP-AEAERDMNSTEKDADSDVWVGADNDYSDNSMVREPEPAEQQEETRPSVVEEEEG 246

Qy 233 EVAEVEEEE-----ADDEDEDGDEVEEEAEPEYEEATERTTSIA 273
 |||: :|| | ||:| ||:| | :| | ||:|

Db 247 EVAQEDDEEEELDTQDGDGEEDHEAADDEEEEDVDEIDAFGESDDVDADEPTTNVA 306

Qy 274 ---TTTTTTTESVEEVVR----- 288
 |||||

Db 307 MTTTTTTTTTTESVEEVVRMFCWAHADTGPCTASMPSWYFDAVDGRTMYELMYGGCGNMN 366

Qy 289 -----VPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQ 333
 ||| |:|||| | ||| ||||| |||||

Db 367 NFESEYCLSVCSVVPTDMPSSPDAVDHYLETADENEHAHFQKAKESLEAKHRERMSQ 426

Qy 334 VMREWEEAERQAKNLPKADKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDR 393
 |||||:|||| || | ||||:||||:|||||:||||

Db 427 VMREWEEAERQAKNLPKADKAVIQHFQEKVESLEQEAANERQQLVETHMARVEALLNDR 486

Qy 394 RRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRS 453
 |||||:|||| | ||||:||||| |||||

Db 487 RRLALENYLTALQQDPPRPRHVFSLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRP 546

Qy 454 QVMTHLRVIYERMNQSLSLYNVPAVAEEIQDEVDLLQKEQNYSDDLANMISEPRISY 513
 |:|||| | |||| || | ||:|:| | ||:| | ||: :| :|

Db 547 QVLTHLRVIEERMNQSLGLLYKVPGVADDIQDQV-ELLQREQAEMAQQLANLQTDVRVSY 605

Qy 514 GNDALMPSLTETKTTVELLPVNGEFLDDLQPDWH--SFGADSVPAANTENEVEPVDPARPA 571
 ||||| :|| | :| : | || | ||:||||:|

Db 606 GNDALMPDQELGDGQADLLP--QEDTLGGVGFVHPESFN---QLNTENQVEPVDSRPTF 659

Qy 572 DRGLTTRPGSGLTNIKTEEISEVNLDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLM 631
 :||: ||| :| | :| : :| | : |||||

Db 660 ERGVPTRP--VTGKSMEAVPELRMETEDRQSTEYEVHHQKLVFFAEDVGSNKGAIIGLM 716

Qy 632 VGGVVIATVIVITLVMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFE 691
 |||||:|||||:|||||:|||||

Db 717 VGGVVIATVIVITLVMLRKKQYTSIHGGIIEVDAAVTPEERHLSKMQQNGYENPTYKFFE 776

Qy 692 QMQN 695
 ||||

Db 777 QMQN 780

RESULT 9

A4_FUGRU

ID A4_FUGRU STANDARD; PRT; 737 AA.

AC 093279;

DT 10-OCT-2003 (Rel. 42, Created)

DT 10-OCT-2003 (Rel. 42, Last sequence update)

DT 10-OCT-2003 (Rel. 42, Last annotation update)

DE Alzheimer's disease amyloid A4 protein homolog precursor [Contains:

DE Beta-amyloid protein (Beta-APP) (A-beta)].

GN APP.

OS Fugu rubripes (Japanese pufferfish) (Takifugu rubripes).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Actinopterygii; Neopterygii; Teleostei; Euteleostei; Neoteleostei;
 OC Acanthomorpha; Acanthopterygii; Percomorpha; Tetraodontiformes;
 OC Tetradontoidea; Tetraodontidae; Takifugu.
 OX NCBI_TaxID=31033;
 RN [1]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=98252138; PubMed=9599080;
 RA Villard L., Tassone F., Crnogorac-Jurcevic T., Clancy K., Gardiner K.;
 RT "Analysis of pufferfish homologues of the AT-rich human APP gene.";
 RL Gene 210:17-24(1998).
 CC -!- FUNCTION: Functional neuronal receptor which couples to
 CC intracellular signaling pathway through the GTP-binding protein
 CC G(O) (By similarity).
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein.
 CC -!- SIMILARITY: Belongs to the APP family.
 CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
 CC -----
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
 CC the European Bioinformatics Institute. There are no restrictions on its
 CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by and for commercial
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
 CC or send an email to license@isb-sib.ch).
 CC -----
 DR EMBL; AF090120; AAD13392.1; -.
 DR HSSP; P05067; 1HZ3.
 DR InterPro; IPR008155; A4_APP.
 DR InterPro; IPR008154; A4_extra.
 DR InterPro; IPR001255; Beta-APP.
 DR InterPro; IPR002223; Kunitz_BPTI.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR Pfam; PF03494; Beta-APP; 1.
 DR Pfam; PF00014; Kunitz_BPTI; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR PRINTS; PR00759; BASICPTASE.
 DR ProDom; PD000222; Kunitz_BPTI; 1.
 DR SMART; SM00006; A4_EXTRA; 1.
 DR SMART; SM00131; KU; 1.
 DR PROSITE; PS00319; A4_EXTRA; FALSE_NEG.
 DR PROSITE; PS00320; A4_INTRA; 1.
 DR PROSITE; PS00280; BPTI_KUNITZ_1; 1.
 DR PROSITE; PS50279; BPTI_KUNITZ_2; 1.
 KW Glycoprotein; Amyloid; Neurone; Transmembrane; Signal;
 KW Serine protease inhibitor.
 FT SIGNAL 1 18 POTENTIAL.
 FT CHAIN 19 737 ALZHEIMER'S DISEASE AMYLOID A4
 FT PROTEIN HOMOLOG.
 FT CHAIN 639 681 BETA-AMYLOID PROTEIN (POTENTIAL).
 FT DOMAIN 19 668 EXTRACELLULAR (POTENTIAL).
 FT TRANSMEM 669 689 POTENTIAL.
 FT DOMAIN 690 737 CYTOPLASMIC (POTENTIAL).
 FT DOMAIN 286 344 BPTI/KUNITZ INHIBITOR.
 FT SITE 726 729 CLATHRIN-BINDING (BY SIMILARITY).
 FT ACT_SITE 300 301 REACTIVE BOND.

FT DISULFID 290 340 BY SIMILARITY.
 FT DISULFID 299 323 BY SIMILARITY.
 FT DISULFID 315 336 BY SIMILARITY.
 FT CARBOHYD 522 522 N-LINKED (GLCNAC. . .) (POTENTIAL).
 SQ SEQUENCE 737 AA; 82856 MW; 6FAD01E2E3B2B7E2 CRC64;

Query Match 67.0%; Score 2446.5; DB 1; Length 737;
 Best Local Similarity 64.0%; Pred. No. 7e-113;
 Matches 482; Conservative 83; Mismatches 101; Indels 87; Gaps 12;

Qy 7 LLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGKTCTIDTK 66
 :||| | :| :| | ||| |||:||||:||||:|||||:|||||:|:|
 Db 8 VLLLVATLRSSEIPADDTVGLLTPQVAMFCGKLNMHINVQNGKWESDPSGKTKSCLNTK 67

Qy 67 EGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVGEFVSDA 126
 |||||:|||||:||||:| | |:|||||
 Db 68 EGILQYCQEVPELQITNVVEANQPVSIQNWCKKGRKQCRSHTHIVVPYRCLVGEFVSDA 127

Qy 127 LLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDKFRGVEFVC 186
 |||||: ||:|||||:| ::| |||||:||||:|
 Db 128 LLVPDKCKFLHQERMNQCESHLHWHTVAKESCGDRSMNLHDYGMLLPCGIDRFRGVKFVC 187

Qy 187 CPLAEESDNVDSADAEEDSDVWGGADTDYADGS---EDKVVEVAEEEEVAEVEEEAD 243
 || || ||:: | ::||| |||:|:: | : ||: | :| |
 Db 188 CP-AETEQETDSSEVEGEESDVWGGADPEYSENSPPTPSRATYVAGD---AFERDENG 243

Qy 244 DDEDEDGDEVEEEAEPYEEATERTTSIA--TTTTTTTSESVEEVVR----- 288
 |||:| :|: | :| ||| ::| |||||
 Db 244 GDEDEDEDVDPTDE---QESDERTANVAMTTTTTTTTTSESVEEVVRVAVCWAQAESGPCR 300

Qy 289 -----VPTTAASTPDAVDKYLE 305
 :|| | | |||:| |
 Db 301 AMLERWYFNPKKRRCVPFLFGGCGGNRNNFESEYCLAVCSSSLPTVAPSPDPAVDQYFE 360

Qy 306 TPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEKVE 365
 |||:|||| |:||| |||||:|||||:|||||
 Db 361 APGDDNEHADFRKAKESLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVIQHFQEKVE 420

Qy 366 SLEQEAAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFNMLKKYVRA 425
 :||||| |||||:| ||| |||: ||| ||| | | :|
 Db 421 ALEQEAAAGERQQLVETHMARVEALLNSRRRLTLENYLGALQANPPRARQVLSLLKKYVRA 480

Qy 426 EQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVPAVAEEIQD 485
 |||||:|||| ||||| ||:|||| |||||:| ||:| |||:
 Db 481 EQKDRQHTLKHFEHVRTVDPKKAAQIRPQVLTHLRVIDERMNQSLSLLYKVPVASEIQN 540

Qy 486 EVDELLQKEQNYSDVLANMIS---EPRISYGNDALMPSLTETKTTVELLPVNGEFSLDD 542
 :: : | : : : : ||||| : : : | :| | :|
 Db 541 QIYPAAGSD---CKDPVEHCVCQVDGLVSYGNDALMPDQAYSSAPMD-MGVDGLGSID- 595

Qy 543 LQPWHSFGADSVANTENEVEPVDPARPAADRGLTTRPGSGLTNIKTEEISEVNLDAEFRH 602
 || |||| ||||| ||| ||| ::::| ||: || : : |
 Db 596 ----QSFN----QANTENHVEPVDPARPIPDRGLPTRP---VSSLKLEEMPEVRTETDKRQ 644

Qy 603 DSGYEVHHQKLFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLKKKQYTSIHGVE 662
 :||||:|||||:|||||:|||||:|||||:|||||:|
 Db 645 SAGYEVYHQKLFFADDVGSNKGAIIGLMVGGVVIATVIVITLVMLRKKQYTSIHGVIE 704

Qy 663 VDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN 695
 |||||:|||||
 Db 705 VDAAVTPEERHLARMQQQNGYENPTYKFFEQMQN 737

RESULT 10

APP2_MOUSE

ID APP2_MOUSE STANDARD; PRT; 695 AA.
 AC Q06335;
 DT 01-JUN-1994 (Rel. 29, Created)
 DT 01-FEB-1996 (Rel. 33, Last sequence update)
 DT 15-MAR-2004 (Rel. 43, Last annotation update)
 DE Amyloid-like protein 2 precursor (CDEI-box binding protein) (CDEBP).
 GN APLP2.
 OS Mus musculus (Mouse).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
 OX NCBI_TaxID=10090;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC TISSUE=Fetal brain;
 RA von der Kammer H.;
 RL Submitted (JUL-1994) to the EMBL/GenBank/DDBJ databases.
 RN [2]
 RP SEQUENCE OF 1-246 FROM N.A.
 RX MEDLINE=94032480; PubMed=8218408;
 RA Hanes J., von der Kammer H., Kristjansson G.I., Scheit K.H.;
 RT "The complete cDNA coding sequence for the mouse CDEI binding
 RT protein.";
 RL Biochim. Biophys. Acta 1216:154-156(1993).
 RN [3]
 RP SEQUENCE OF 185-695 FROM N.A.
 RC STRAIN=BALB/c; TISSUE=Heart;
 RX MEDLINE=93129193; PubMed=1482349;
 RA Vidal F., Blangy A., Rassoulzadegan M., Cuzin F.;
 RT "A murine sequence-specific DNA binding protein shows extensive local
 RT similarities to the amyloid precursor protein.";
 RL Biochem. Biophys. Res. Commun. 189:1336-1341(1992).
 RN [4]
 RP SEQUENCE OF 1-35 FROM N.A.
 RC STRAIN=129/Sv;
 RX MEDLINE=96029629; PubMed=7592716;
 RA von Koch C.S., Lahiri D.K., Mammen A.L., Copeland N.G.,
 RA Gilbert D.J., Jenkins N.A., Sisodia S.S.;
 RT "The mouse APLP2 gene. Chromosomal localization and promoter
 RT characterization.";
 RL J. Biol. Chem. 270:25475-25480(1995).
 CC -!- FUNCTION: Binds to the DNA 5'-GTCACATG-3' (CDEI box) which plays
 CC an important role in the early development of embryos.
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein and nuclear
 CC (Potential).
 CC -!- SIMILARITY: Belongs to the APP family.

 CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
 CC the European Bioinformatics Institute. There are no restrictions on its

CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
CC or send an email to license@isb-sib.ch).

CC -----
DR EMBL; Z22592; CAA80306.1; -.
DR EMBL; M97216; AAA20039.1; -.
DR EMBL; U34291; AAC52318.1; -.
DR PIR; JC1404; JC1404.
DR PIR; S38344; S38344.
DR HSSP; P05067; 1MWP.
DR MGD; MGI:88047; Aplp2.
DR InterPro; IPR008155; A4_APP.
DR InterPro; IPR008154; A4_extra.
DR Pfam; PF02177; A4_EXTRA; 1.
DR PRINTS; PR00203; AMYLOIDA4.
DR SMART; SM00006; A4_EXTRA; 1.
DR PROSITE; PS00319; A4_EXTRA; 1.
DR PROSITE; PS00320; A4_INTRA; 1.
KW Transmembrane; DNA-binding; Signal; Nuclear protein.
FT SIGNAL 1 29 POTENTIAL.
FT CHAIN 30 695 AMYLOID-LIKE PROTEIN 2.
FT DOMAIN 30 624 EXTRACELLULAR (POTENTIAL).
FT TRANSMEM 625 648 POTENTIAL.
FT DOMAIN 649 695 CYTOPLASMIC (POTENTIAL).
FT DOMAIN 218 294 ASP/GLU-RICH (HIGHLY ACIDIC).
FT DOMAIN 218 231 POLY-GLU.
FT DOMAIN 256 266 POLY-GLU.
FT CARBOHYD 485 485 N-LINKED (GLCNAC. . .) (POTENTIAL).
FT CONFLICT 185 189 GMLLP -> MACCC (IN REF. 3).
SQ SEQUENCE 695 AA; 78944 MW; BBF4B95AAB2A0311 CRC64;

Query Match 47.4%; Score 1730; DB 1; Length 695;
Best Local Similarity 49.0%; Pred. No. 7.9e-78;
Matches 358; Conservative 119; Mismatches 163; Indels 90; Gaps 19;

Qy 5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWDSDP 56
| :||| || | : ||| :||||| ||:||||:| | ||: ||
Db 15 LLVLLLLGLTAPAAALAGYIEALAANAGTGFVAEAPQIAMLCGKLNMHVNIQTGKWEPPD 74

Qy 57 SGTKTCTIDTKEGILQYCQEVPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
:||||:| ||| :|||||:|||||:||||| | :||:| :|||: | |||:
Db 75 TGTKSCLGTKEEVQYCQEIYPELQITNVMEANQPVNIDSWCRRDKRQCKS--HIVIPFK 132

Qy 117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176
||||||| |||| |:| ||||:|||| | |||: || | : |: |||||:
Db 133 CLVGEFVSDVLLVPDNCQFFHQERMEVCEKHQRWHTLVKEACLTEGLTLYSYGMLLPCGV 192

Qy 177 DKFRGVFVCCPLAE--ESDNVDSADAEEDSDVWWGGADTDYADGSEDKVVEVAE---E 231
|:| | |:|||| : :||: | :||: | | || : :| |
Db 193 DQFHGTEYVCCPQTKTVDSSTMSKEEEEEEE-----DEEDEEDYDLKSEFPTE 243

Qy 232 EEVAEVEEEEEAD-DEDEDGDEVEEEAE-----EPYEEATERTTSIATTTTTTTTES 282
: : | || :||:|:|:| | : : : | | | | : : | : :
Db 244 ADLEDFTAAADEEEEEDEEGEEVVEDRDYYYDPFKGDDYNE--ENPTSPSSEGTISDK 301

Qy 283 VEEVVRVPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAE 342

[illegible]

```

RESULT 11
APP2_HUMAN
ID APP2_HUMAN STANDARD; PRT; 763 AA.
AC Q06481;
DT 01-JUN-1994 (Rel. 29, Created)
DT 01-OCT-1996 (Rel. 34, Last sequence update)
DT 15-MAR-2004 (Rel. 43, Last annotation update)
DE Amyloid-like protein 2 precursor (Amyloid protein homolog) (APPH)
DE (CDEI-box binding protein) (CDEBP).
GN APLP2 OR APPL2.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX NCBI_TaxID=9606;
RN [1]
RP SEQUENCE FROM N.A.
RC TISSUE=Placenta;
RX MEDLINE=93250009; PubMed=8485127;
RA Sprecher C.A., Grant F.J., Grimm G., O'Hara P.J., Norris F.,
RA Norris K., Foster D.C.;
RT "Molecular cloning of the cDNA for a human amyloid precursor protein
RT homolog: evidence for a multigene family.";
RL Biochemistry 32:4481-4486(1993).
RN [2]
RP SEQUENCE FROM N.A.

```

RC TISSUE=Ovary;
 RX MEDLINE=95217334; PubMed=7702756;
 RA von der Kammer H., Hanes J., Klaudiny J., Scheit K.H.;
 RT "A human amyloid precursor-like protein is highly homologous to a
 RT mouse sequence-specific DNA-binding protein.";
 RL DNA Cell Biol. 13:1137-1143(1994).
 RN [3]
 RP SEQUENCE FROM N.A.
 RC TISSUE=Brain;
 RX MEDLINE=94035131; PubMed=8220435;
 RA Wasco W., Gurubhagavatula S., Paradis M., Romano D.M., Sisodia S.S.,
 RA Hyman B.T., Neve R.L., Tanzi R.E.;
 RT "Isolation and characterization of APLP2 encoding a homologue of the
 RT Alzheimer's associated amyloid beta protein precursor.";
 RL Nat. Genet. 5:95-99(1993).
 RN [4]
 RP SEQUENCE FROM N.A. (ISOFORM 3).
 RC TISSUE=Lung;
 RX MEDLINE=22388257; PubMed=12477932;
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
 RT "Generation and initial analysis of more than 15,000 full-length
 RT human and mouse cDNA sequences.";
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
 CC -!- FUNCTION: May play a role in the regulation of hemostasis. The
 CC soluble form may have inhibitory properties towards coagulation
 CC factors. May interact with cellular G-protein signaling pathways.
 CC May bind to the DNA 5'-GTCACATG-3' (CDEI box).
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein and nuclear
 CC (Potential).
 CC -!- ALTERNATIVE PRODUCTS:
 CC Event=Alternative splicing; Named isoforms=3;
 CC Comment=Additional isoforms seem to exist;
 CC Name=1;
 CC IsoId=Q06481-1; Sequence=Displayed;
 CC Name=2;
 CC IsoId=Q06481-2; Sequence=VSP_000018;
 CC Name=3;
 CC IsoId=Q06481-3; Sequence=VSP_000019;
 CC -!- TISSUE SPECIFICITY: In placenta, brain, heart, lung, liver, kidney
 CC and endothelial tissues.
 CC -!- SIMILARITY: Belongs to the APP family.

```

CC  -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC  -----
CC  This SWISS-PROT entry is copyright. It is produced through a collaboration
CC  between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC  the European Bioinformatics Institute. There are no restrictions on its
CC  use by non-profit institutions as long as its content is in no way
CC  modified and this statement is not removed. Usage by and for commercial
CC  entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC  or send an email to license@isb-sib.ch).
CC  -----
DR  EMBL; S60099; AAC60589.1; -.
DR  EMBL; L09209; AAA35526.1; -.
DR  EMBL; Z22572; CAA80295.1; -.
DR  EMBL; L27631; AAC41701.1; -.
DR  EMBL; BC000373; AAH00373.1; -.
DR  PIR; A49321; A49321.
DR  HSSP; P05067; 1MWP.
DR  Genew; HGNC:598; APLP2.
DR  MIM; 104776; -.
DR  GO; GO:0016021; C:integral to membrane; NAS.
DR  GO; GO:0005634; C:nucleus; IDA.
DR  GO; GO:0003677; F:DNA binding; NAS.
DR  GO; GO:0007186; P:G-protein coupled receptor protein signalin. . .; NAS.
DR  InterPro; IPR008155; A4_APP.
DR  InterPro; IPR008154; A4_extra.
DR  InterPro; IPR002223; Kunitz_BPTI.
DR  Pfam; PF02177; A4_EXTRA; 1.
DR  Pfam; PF00014; Kunitz_BPTI; 1.
DR  PRINTS; PR00203; AMYLOIDA4.
DR  PRINTS; PR00759; BASICPTASE.
DR  ProDom; PD000222; Kunitz_BPTI; 1.
DR  SMART; SM00006; A4_EXTRA; 1.
DR  SMART; SM00131; KU; 1.
DR  PROSITE; PS00319; A4_EXTRA; 1.
DR  PROSITE; PS00320; A4_INTRA; 1.
DR  PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR  PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW  Transmembrane; Signal; Alternative splicing; DNA-binding;
KW  Nuclear protein; Serine protease inhibitor.
FT  SIGNAL      1      29      POTENTIAL.
FT  CHAIN       30     763     AMYLOID-LIKE PROTEIN 2.
FT  DOMAIN      30     692     EXTRACELLULAR (POTENTIAL).
FT  TRANSMEM    693     716     POTENTIAL.
FT  DOMAIN      717     763     CYTOPLASMIC (POTENTIAL).
FT  DOMAIN      215     280     ASP/GLU-RICH (HIGHLY ACIDIC).
FT  DOMAIN      306     364     BPTI/KUNITZ INHIBITOR.
FT  DOMAIN      215     231     POLY-GLU.
FT  ACT_SITE    320     321     REACTIVE BOND (BY SIMILARITY).
FT  DISULFID    310     360     BY SIMILARITY.
FT  DISULFID    319     343     BY SIMILARITY.
FT  DISULFID    335     356     BY SIMILARITY.
FT  VARSPLIC    308     363     Missing (in isoform 2).
FT                                     /FTId=VSP_000018.
FT  VARSPLIC    613     624     Missing (in isoform 3).
FT                                     /FTId=VSP_000019.
FT  CONFLICT    543     543     S -> I (IN REF. 1).
SQ  SEQUENCE    763 AA;  86955 MW;  CA3A7D6DDB8A28D0 CRC64;

```

Query Match 47.2%; Score 1725; DB 1; Length 763;
Best Local Similarity 46.9%; Pred. No. 1.6e-77;
Matches 369; Conservative 112; Mismatches 170; Indels 136; Gaps 19;

```
Qy      5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWDSDP 56
      | | | | | | | | | | : | | | | | : | | | | | | | | | | | | | | | | |
Db     15 LLLLLLVGLTAPALALAGYIEALAANAGTGFAVAEPQIAMFCGKLNMHVNIQTGWEPDP 74

Qy     57 SGTKTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
      : | | | : | | | : | | | | | : | | | | | : | | | | | : | | | : |
Db     75 TGTKSCFETKEEVLYCQEMYPELQITNVMEANQRVSIDNWCRRDKKQCKS--RFVTPFK 132

Qy    117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176
      | | | | | | | | | | : | | | : | | | : | | | | | | | | : | | | | | :
Db    133 CLVGEFVSDVLLVPEKCQFFHKERMEVCENHQHWHTVVKEACLTQGMTLYSYGMLLPCGV 192

Qy    177 DKFRGVEFVCCPLAEESDNVDSADAEEDDSDVWGGADTDYADGSEDKVVEVAEEEEVAE 236
      | : | | | : | | | : | | | : | | | : | | | : | | | : | | | :
Db    193 DQFHGTEYVCCPQTKIIGSVSKEEEEEDEE-----EEEEDEEEDYDVYKSEFPTEAD 245

Qy    237 VEE--EEA--DDDEDDDEDGDEVEEEAAEPPY-----EEATERTTSIATTTTTTTES 282
      : | : | | : | | | : | | | : | | | : | | | : | | | : | | | :
Db    246 LEDFTEAAVDEDDDEEEGEEVVEDRDYYYDTFKGDDYNEENPTEPGSDGTMSDKEITHD 305

Qy    283 VEEV-----VRVP 290
      | : | | | | | | | | | | | | | | | | | | | | | | | | | | | |
Db    306 VKAVCSQEAMTGPCRAVMPRWYFDLSKGKCVRFIYGCGGNRNNFESEDYCMVCKAMIP 365

Qy    291 TTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEEAERQAKNLPK 350
      | | | | | | | | | | : | | | | | | | | | | : | | | | | : | | | | |
Db    366 PTPLPTND-VDVYFETSADDNEHARFQKAKEQLEIRHRNRMDRVKKEWEEAELQAKNLPK 424

Qy    351 ADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPP 410
      | : : : | | | | | : : | | | : : | | | : : | | | : : | | | : |
Db    425 AERQTLIQHFQAMVKALEKEAASEKQQLVETHLARVEAMLNDRRRMALENYLAALQSDPP 484

Qy    411 RPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSL 470
      | | : | : | | | | | | | | | : | | | : | | | : | | | : | | | |
Db    485 RPHRILQALRRYVRAENKDRLHTIRHYQHVLAVDPEKAAQMKSQVMTHLHVIEERNQSL 544

Qy    471 SLLYNVPAVAEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDAIMPSTLTETKTVE 530
      | | | | | | | | | : | | | : | | | : | | | : | | | : | | | :
Db    545 SLLYKVPYVAQEIQEEIDELLQEQR-----ADM-----DQFTASISETPVDVR 587

Qy    531 LLPVNGEFSLDDLQPWHSFGADSVANTENEVEPVDARPAADRGLTTRPG-----SGLTN 585
      | : | | : : | : | | | | | | | | | : | | : | | | | |
Db    588 ---VSSEES-EEIPPFHPF--HPFPALPENE----DTQPELYHPMKKSGVGEQDGGGLIG 637

Qy    586 IKTEEISEVN-LDAEFRHDSGYEVHHQKLVFFAEDVGS-----NKGAI 627
      : : | : | : | | | : | : : : | | | | | : | :
Db    638 AEEKVINSKNKVDENMVIDETLDV--KEMIFNAERVGGLEEEERESVGPLREDFSLSSAL 695

Qy    628 IGLMVGGVVIATVIVITLVMLKKKQYTSIHGGVVEVDAAVTPEERHLSKMQQNGYENPTY 687
      | | | : | | | | | | : | | | : | | | : | | | : | | | : | | |
Db    696 IGLLVIAVAIATVIVISLVMLRKRQYGTISHGIVEVDPMLTPEERHLNKMQNHYENPTY 755
```

Qy 688 KFFEQQ 694
 |: ||||
Db 756 KYLEQQ 762

RESULT 12

APP2_RAT

ID APP2_RAT STANDARD; PRT; 765 AA.
AC P15943;
DT 01-APR-1990 (Rel. 14, Created)
DT 01-OCT-1996 (Rel. 34, Last sequence update)
DT 28-FEB-2003 (Rel. 41, Last annotation update)
DE Amyloid-like protein 2 precursor (Sperm membrane protein YWK-II).
GN APLP2.
OS Rattus norvegicus (Rat).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX NCBI_TaxID=10116;
RN [1]
RP SEQUENCE OF 1-627 FROM N.A.
RC STRAIN=Wistar; TISSUE=Brain, and Heart;
RX MEDLINE=94368849; PubMed=8086458;
RA Sandbrink R., Masters C.L., Beyreuther K.;
RT "Complete nucleotide and deduced amino acid sequence of rat amyloid
RT protein precursor-like protein 2 (APLP2/APPH): two amino acids length
RT difference to human and murine homologues.";
RL Biochim. Biophys. Acta 1219:167-170(1994).
RN [2]
RP SEQUENCE OF 575-765 FROM N.A.
RC TISSUE=Testis;
RX MEDLINE=90207205; PubMed=1690887;
RA Yan Y.C., Bai Y., Wang L.F., Miao S.Y., Koide S.S.;
RT "Characterization of cDNA encoding a human sperm membrane protein
RT related to A4 amyloid protein.";
RL Proc. Natl. Acad. Sci. U.S.A. 87:2405-2408(1990).
CC -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC -!- ALTERNATIVE PRODUCTS:
CC Event=Alternative splicing; Named isoforms=4;
CC Name=A;
CC IsoId=P15943-1; Sequence=Displayed;
CC Name=B;
CC IsoId=P15943-2; Sequence=VSP_000021;
CC Name=C;
CC IsoId=P15943-3; Sequence=VSP_000020;
CC Name=D;
CC IsoId=P15943-4; Sequence=VSP_000020, VSP_000021;
CC -!- SIMILARITY: Belongs to the APP family.
CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.

CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
CC or send an email to license@isb-sib.ch).
CC -----

DR EMBL; X77934; CAA54906.1; -.
 DR EMBL; M31322; AAA42352.1; -.
 DR PIR; A35981; A35981.
 DR PIR; S42880; S42880.
 DR HSSP; P05067; 1MWP.
 DR InterPro; IPR008155; A4_APP.
 DR InterPro; IPR008154; A4_extra.
 DR InterPro; IPR002223; Kunitz_BPTI.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR Pfam; PF00014; Kunitz_BPTI; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR PRINTS; PR00759; BASICPTASE.
 DR ProDom; PD000222; Kunitz_BPTI; 1.
 DR SMART; SM00006; A4_EXTRA; 1.
 DR SMART; SM00131; KU; 1.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 DR PROSITE; PS00280; BPTI_KUNITZ_1; 1.
 DR PROSITE; PS50279; BPTI_KUNITZ_2; 1.
 KW Transmembrane; Alternative splicing; Serine protease inhibitor;
 KW Signal; Glycoprotein.
 FT SIGNAL 1 29 POTENTIAL.
 FT CHAIN 30 765 AMYLOID-LIKE PROTEIN 2.
 FT DOMAIN 30 695 EXTRACELLULAR (POTENTIAL).
 FT TRANSMEM 696 718 POTENTIAL.
 FT DOMAIN 719 765 CYTOPLASMIC (POTENTIAL).
 FT DOMAIN 218 282 ASP/GLU-RICH (HIGHLY ACIDIC).
 FT DOMAIN 308 366 BPTI/KUNITZ INHIBITOR.
 FT ACT_SITE 322 323 REACTIVE BOND (BY SIMILARITY).
 FT DISULFID 312 362 BY SIMILARITY.
 FT DISULFID 321 345 BY SIMILARITY.
 FT DISULFID 337 358 BY SIMILARITY.
 FT DOMAIN 218 229 POLY-GLU.
 FT CARBOHYD 628 628 O-LINKED (GLYCOSAMINOGLYCAN) (POTENTIAL).
 FT VARSPLIC 311 365 Missing (in isoform C and isoform D).
 FT /FTid=VSP_000020.
 FT VARSPLIC 616 627 Missing (in isoform B and isoform D).
 FT /FTid=VSP_000021.
 FT CONFLICT 575 577 DQF -> EFV (IN REF. 2).
 SQ SEQUENCE 765 AA; 86882 MW; CF51FCCCE305A0CF CRC64;

Query Match 46.8%; Score 1709; DB 1; Length 765;
 Best Local Similarity 45.9%; Pred. No. 9.5e-77;
 Matches 361; Conservative 124; Mismatches 168; Indels 134; Gaps 20;

Qy 5 LALLLLAAWTARALEV-----PTDGNAG---LLAEPQIAMFCGRLNMHMNVQNGKWSDSP 56
 | :||| || | : ||| :|||||||:||||:|:| |||: ||
 Db 15 LLVLLLLGLTAPAAALAGYIEALANAGTGFAVAEPQIAMFCGKLNHVNITGKWEPPDP 74
 Qy 57 SGTKTCTIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYR 116
 :|||:|: ||| :|||||:|||||||:||||| | :||:| :|||:| | |||:|
 Db 75 TGTKSCLGTKEEVLQYCQEIYPELQITNVMEANQPVNIDSWCRRDKKQCRS--HIVIPFK 132
 Qy 117 CLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGI 176
 ||||| ||||: |:| ||||: ||| | |||| || | : | : |||||:|
 Db 133 CLVGEFVSDVLLVPENCQFFHQERMEVCEKHQRWHTVVKEACLTEGMTLYSYGMLLPCGV 192

OX NCBI_TaxID=9606;
 RN [1]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=98088960; PubMed=9428684;
 RA Paliga K., Peraus G., Kreger S., Duwrrwang U., Hesse L., Multhaup G.,
 RA Masters C.L., Beyreuther K., Weidemann A.;
 RT "Human amyloid precursor-like protein 1 -- cDNA cloning, ectopic
 RT expression in COS-7 cells and identification of soluble forms in the
 RT cerebrospinal fluid.";
 RL Eur. J. Biochem. 250:354-363(1997).
 RN [2]
 RP SEQUENCE FROM N.A.
 RX MEDLINE=98180887; PubMed=9521588;
 RA Lenkkeri U., Kestila M., Lamerdin J., McCready P., Adamson A.,
 RA Olsen A., Tryggvason K.;
 RT "Structure of the human amyloid-precursor-like protein gene APLP1 at
 RT 19q13.1.";
 RL Hum. Genet. 102:192-196(1998).
 RN [3]
 RP SEQUENCE FROM N.A.
 RC TISSUE=Ovary;
 RX MEDLINE=22388257; PubMed=12477932;
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
 RT "Generation and initial analysis of more than 15,000 full-length
 RT human and mouse cDNA sequences.";
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
 RN [4]
 RP POSSIBLE FUNCTION, AND TISSUE SPECIFICITY.
 RX MEDLINE=96115107; PubMed=7494461;
 RA Kim T.-W., Wu K., Xu J.-L., McAuliffe G., Tanzi R.E., Wasco W.,
 RA Black I.B.;
 RT "Selective localization of amyloid precursor-like protein 1 in the
 RT cerebral cortex postsynaptic density.";
 RL Brain Res. Mol. Brain Res. 32:36-44(1995).
 RN [5]
 RP HEPARIN AND ZINC BINDING.
 RX MEDLINE=95014513; PubMed=7929392;
 RA Bush A.I., Pettingell W.H. Jr., de Paradis M., Tanzi R.E., Wasco W.;
 RT "The amyloid beta-protein precursor and its mammalian homologues.
 RT Evidence for a zinc-modulated heparin-binding superfamily.";
 RL J. Biol. Chem. 269:26618-26621(1994).

RN [6]
RP INTERACTION WITH APBA2.
RX MEDLINE=99107877; PubMed=9890987;
RA Tomita S., Ozaki T., Taru H., Oguchi S., Takeda S., Yagi Y.,
RA Sakiyama S., Kirino Y., Suzuki T.;
RT "Interaction of a neuron-specific protein containing PDZ domains with
RT Alzheimer's amyloid precursor protein.";
RL J. Biol. Chem. 274:2243-2254(1999).

RN [7]
RP EXTRACELLULAR COPPER-BINDING.
RX MEDLINE=22130992; PubMed=12135352;
RA Simons A., Ruppert T., Schmidt C., Schlicksupp A., Pipkorn R.,
RA Reed J., Masters C.L., White A.R., Cappai R., Beyreuther K.,
RA Bayer T.A., Multhaup G.;
RT "Evidence for a copper-binding superfamily of the amyloid precursor
RT protein.";
RL Biochemistry 41:9310-9320(2000).
CC -!- FUNCTION: May play a role in postsynaptic function. The C-terminal
CC gamma-secretase processed fragment, ALID1, activates transcription
CC activation through APBB1 (Fe65) binding (By similarity). Couples
CC to JIP signal transduction through C-terminal binding. May
CC interact with cellular G-protein signaling pathways. Can regulate
CC neurite outgrowth through binding to components of the
CC extracellular matrix such as heparin and collagen I.
CC -!- FUNCTION: The gamma-CTF peptide, C30, is a potent enhancer of
CC neuronal apoptosis (By similarity).
CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC cytoplasmic proteins, including APBB and APBA family members,
CC MAPK8IP1 and Dab1 (By similarity). Binding to Dab1 inhibits its
CC serine phosphorylation (By similarity).
CC -!- SUBCELLULAR LOCATION: Type I membrane protein. C-terminally
CC processed in the Golgi complex.
CC -!- TISSUE SPECIFICITY: Expressed in the cerebral cortex where it is
CC localized to the postsynaptic density (PSD).
CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
CC phosphorylated proteins is required for the specific binding of
CC the PID domain. However additional amino acids either N- or C-
CC terminal to the NPXY motif are often required for complete
CC interaction. The NPXY site is also involved in clathrin-mediated
CC endocytosis.
CC -!- PTM: Proteolytically cleaved by caspases during neuronal
CC apoptosis. Cleaved, in vitro, at Asp-620 by caspase-3 (By
CC similarity).
CC -!- PTM: N- and O-glycosylated.
CC -!- MISCELLANEOUS: Binds zinc and copper in the extracellular domain.
CC Zinc-binding increases heparin binding. No Cu(II) reducing
CC activity with copper-binding.
CC -!- SIMILARITY: Belongs to the APP family.

CC -----
CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
CC or send an email to license@isb-sib.ch).
CC -----

RC TISSUE=Brain;
 RX MEDLINE=93066322; PubMed=1279693;
 RA Wasco W., Bupp K., Magendantz M., Gusella J.F., Tanzi R.E.,
 RA Solomon F.;
 RT "Identification of a mouse brain cDNA that encodes a protein related
 RT to the Alzheimer disease-associated amyloid beta protein precursor.";
 RL Proc. Natl. Acad. Sci. U.S.A. 89:10758-10762(1992).
 RN [2]
 RP SEQUENCE FROM N.A.
 RC TISSUE=Retina;
 RX MEDLINE=22388257; PubMed=12477932;
 RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
 RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
 RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
 RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
 RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
 RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
 RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
 RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
 RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
 RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
 RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
 RA Fahey J., Helton E., Kettelman M., Madan A., Rodrigues S., Sanchez A.,
 RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
 RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
 RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
 RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
 RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
 RT "Generation and initial analysis of more than 15,000 full-length
 RT human and mouse cDNA sequences.";
 RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
 RN [3]
 RP COLLAGEN-BINDING.
 RX MEDLINE=96139497; PubMed=8576160;
 RA Beher D., Hesse L., Masters C.L., Multhaup G.;
 RT "Regulation of amyloid protein precursor (APP) binding to collagen and
 RT mapping of the binding sites on APP and collagen type I.";
 RL J. Biol. Chem. 271:1613-1620(1996).
 RN [4]
 RP INTERACTION WITH DAB1.
 RX MEDLINE=99389880; PubMed=10460257;
 RA Homayouni R., Rice D.S., Sheldon M., Curran T.;
 RT "Disabled-1 binds to the cytoplasmic domain of amyloid precursor-like
 RT protein 1.";
 RL J. Neurosci. 19:7507-7515(1999).
 RN [5]
 RP INTERACTION WITH MAPK8IP1.
 RX MEDLINE=21408156; PubMed=11517249;
 RA Matsuda S., Yasukawa T., Homma Y., Ito Y., Niikura T., Hiraki T.,
 RA Hirai S., Ohno S., Kita Y., Kawasumi M., Kouyama K., Yamamoto T.,
 RA Kyriakis J.M., Nishimoto I.;
 RT "C-jun N-terminal kinase (JNK)-interacting protein-1b/islet-brain-1
 RT scaffolds Alzheimer's amyloid precursor protein with JNK.";
 RL J. Neurosci. 21:6597-6607(2001).
 RN [6]
 RP GAMMA-SECRETASE PROCESSING, INTERACTION WITH APBB1, AND MUTAGENESIS OF
 RP TYR-641.

RX MEDLINE=22313598; PubMed=12228233;
 RA Scheinfeld M.H., Ghersi E., Laky K., Fowlkes B.J., D'Adamio L.;
 RT "Processing of beta-amyloid precursor-like protein-1 and -2 by gamma-
 RT secretase regulates transcription.";
 RL J. Biol. Chem. 277:44195-44201(2002).
 CC -!- FUNCTION: May play a role in postsynaptic function. The C-terminal
 CC gamma-secretase processed fragment, ALID1, activates transcription
 CC activation through APBB1 (Fe65) binding. Couples to JIP signal
 CC transduction through C-terminal binding. May interact with
 CC cellular G-protein signaling pathways. Can regulate neurite
 CC outgrowth through binding to components of the extracellular
 CC matrix such as heparin and collagen I.
 CC -!- FUNCTION: The gamma-CTF peptide, C30, is a potent enhancer of
 CC neuronal apoptosis (By similarity).
 CC -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
 CC cytoplasmic proteins, including APBB and APBA family members,
 CC MAPK8IP1 and Dab1 (By similarity). Binding to Dab1 inhibits its
 CC serine phosphorylation.
 CC -!- SUBCELLULAR LOCATION: Type I membrane protein. C-terminally
 CC processed in the Golgi complex.
 CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
 CC phosphorylated proteins is required for the specific binding of
 CC the PID domain. However additional amino acids either N- or C-
 CC terminal to the NPXY motif are often required for complete
 CC interaction. The NPXY site is also involved in clathrin-mediated
 CC endocytosis.
 CC -!- PTM: Proteolytically cleaved by caspases during neuronal
 CC apoptosis. Cleaved, in vitro, at Asp-623 by caspase-3 (By
 CC similarity).
 CC -!- PTM: N- and O-glycosylated.
 CC -!- MISCELLANEOUS: Binds zinc and copper in the extracellular domain.
 CC Zinc-binding increases heparin binding. No Cu(II) reducing
 CC activity with copper-binding.
 CC -!- SIMILARITY: Belongs to the APP family.
 CC -----
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
 CC the European Bioinformatics Institute. There are no restrictions on its
 CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by and for commercial
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
 CC or send an email to license@isb-sib.ch).
 CC -----
 DR EMBL; L04538; AAA37247.1; -.
 DR EMBL; BC021877; AAH21877.1; -.
 DR PIR; A46362; A46362.
 DR HSSP; P05067; 1MWP.
 DR MGD; MGI:88046; Aplp1.
 DR InterPro; IPR008155; A4_APP.
 DR InterPro; IPR008154; A4_extra.
 DR Pfam; PF02177; A4_EXTRA; 1.
 DR PRINTS; PR00203; AMYLOIDA4.
 DR SMART; SM00006; A4_EXTRA; 1.
 DR PROSITE; PS00319; A4_EXTRA; 1.
 DR PROSITE; PS00320; A4_INTRA; 1.
 KW Apoptosis; Endocytosis; Cell adhesion; Coated pits; Neurone;
 KW Heparin-binding; Metal-binding; Copper; Zinc; Signal; Transmembrane;

KW	Glycoprotein.		
FT	SIGNAL	1	37
FT	CHAIN	38	653
FT	CHAIN	624	653
FT	DOMAIN	38	583
FT	TRANSMEM	584	606
FT	DOMAIN	607	653
FT	DOMAIN	157	177
FT	DOMAIN	203	210
FT	DOMAIN	313	345
FT	DOMAIN	413	444
FT	DOMAIN	445	462
FT	DOMAIN	263	271
FT	DOMAIN	535	538
FT	DOMAIN	601	606
FT	SITE	166	166
FT			
FT	SITE	607	618
FT			
FT	SITE	623	624
FT	SITE	641	644
FT	SITE	643	646
FT	CARBOHYD	464	464
FT	CARBOHYD	554	554
FT	MUTAGEN	641	641
FT	CONFLICT	17	17
SQ	SEQUENCE	653 AA;	72750 MW; 56516DC3EA40E4B0 CRC64;

Query Match 32.4%; Score 1183; DB 1; Length 653;
 Best Local Similarity 39.0%; Pred. No. 4.4e-51;
 Matches 275; Conservative 121; Mismatches 221; Indels 88; Gaps 20;

Qy	1	MLPGLALLLLAAWTARA-LEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPST	59
		: : :	
Db	22	LLP-LSLLLLRAQLAVGNLAVGSPSAEAPGSAQVAGLCGRLTLHRDLRTGRWEPDPQRS	80
Qy	60	KTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHPHF-VIPYRCL	118
		: : : : : :	
Db	81	RRCLLDPQRVLEYCRQMPYELHARVEQAAQAI PMERWCGGTRSGRCAHPHHEVVFFHCL	140
Qy	119	VGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYGMLLPCGIDK	178
		: : :	
Db	141	PGEFVSEALLVPEGCRFLHQERMDQCESSTRHQEAQAEACSSQGLILHGSGMLLPCGSDR	200
Qy	179	FRGVEFVCCPLAEESDNVDSADAEEDSDVW-WGGADTDYADGSEDKVVEVAEEEEVAEV	237
		: : : :	
Db	201	FRGVEYVCCP-PPATPNPSGMAAGDPSTRSWPLGGR----AEGGED-----EEEVESF	248
Qy	238	EEEEADDDDEDEDGDEVEEEAEPEYEEATERTTSIATTTTTTTTESVEEVVRVPTTAASTP	297
		: : : : : :	
Db	249	PQPVDYDFVEPPQAESEEEEEERAPPPSSHTPVMVSRVTPTPR-----PT-----	294
Qy	298	DAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEAAERQAKNLPKADKKAVI	357
		: : : : : : : : :	
Db	295	DGVDVYFGMPGEIGEHEGFLRAKMDLEERRMRQINEVMREWAMADSQSKNLPKADRQALN	354
Qy	358	QHFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITALQAVPPRPRHVFN	417

```

      :|||  ::||:: : |||:||||  || |::||| ||| :: |||  ||:  |
Db      355 EHFQSIQTLEEQVSGERQRLVETHATRVIALINDQRRAALEGFLAALQGDPQAERVLM 414
Qy      418 MLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYERMNQSLSLLYNVP 477
      |:|:|:|:|:|:|:|:|:|:|  ||:| | | | | | | | | | | | |
Db      415 ALRRYLRAEQKEQRHTLRHYQHVAVDPEKAQQMRFOVQTHLQVIEERMNQSGLLDQNP 474
Qy      478 AVAEEIQDEVDELLQKEQNYSDVLANMISEPRISYGNDALMP-SLTETKTTVELLPVNG 536
      :|:|:|:|:|  |||  || :  :  || :| | :| |
Db      475 HLAQELRPQIQELL-----LAEHLGPSEL----DASVPGSSSEDK----- 510
Qy      537 EFSLDDLQPWHSFGADSV PANTENEVEPV DARPAADRGLTTRPGSG-----LTNIKTEEI 591
      |||  ||: :|  |  :| | :  |  || :|  |
Db      511 ----GSLQP-----PESKDDPPVTLP---KGSTDQESSSSGREKLTPLEQYE- 550
Qy      592 SEVNLD AEFRHDSGYEVHH---QKL VFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVML 648
      :|| |  | : |  | :  | :| :|:|  |  :|:|:|:|
Db      551 QKVNASA----PRGF PFHSSDIQRDELAPSGTGVSREALSGLLIMGAGGSLIVLSLLLL 606
Qy      649 -KKKQYTSIH HGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQ 692
      ||| | :| | | | | | | :| ||: | :|:|:| | | | :|
Db      607 RKKKPYGTISHGVVEVD PMLTLEEQLRELQRHGYENPTYRFLEE 651

```

RESULT 15

A4_CAEEL

```

ID      A4_CAEEL          STANDARD;          PRT;    686 AA.
AC      Q10651; Q18583; Q95ZX1;
DT      28-FEB-2003 (Rel. 41, Created)
DT      28-FEB-2003 (Rel. 41, Last sequence update)
DT      28-FEB-2003 (Rel. 41, Last annotation update)
DE      Beta-amyloid-like protein precursor.
GN      APL-1 OR C42D8.8.
OS      Caenorhabditis elegans.
OC      Eukaryota; Metazoa; Nematoda; Chromadorea; Rhabditida; Rhabditoidea;
OC      Rhabditidae; Peloderinae; Caenorhabditis.
OX      NCBI_TaxID=6239;
RN      [1]
RP      SEQUENCE OF 6-686 FROM N.A.
RC      STRAIN=Bristol N2;
RX      MEDLINE=94089766; PubMed=8265668;
RA      Daigle I., Li C.;
RT      "apl-1, a Caenorhabditis elegans gene encoding a protein related to
RT      the human beta-amyloid protein precursor.";
RL      Proc. Natl. Acad. Sci. U.S.A. 90:12045-12049(1993).
RN      [2]
RP      SEQUENCE FROM N.A.
RC      STRAIN=Bristol N2;
RA      Hallsworth K.;
RL      Submitted (MAY-1996) to the EMBL/GenBank/DDBJ databases.
RN      [3]
RP      REVISIONS, AND ALTERNATIVE SPLICING.
RA      Waterston R.;
RL      Submitted (JUN-2001) to the EMBL/GenBank/DDBJ databases.
CC      -!- SUBCELLULAR LOCATION: Type I membrane protein (Potential).
CC      -!- ALTERNATIVE PRODUCTS:
CC          Event=Alternative splicing; Named isoforms=2;

```

```

CC      Name=a;
CC      IsoId=Q10651-1; Sequence=Displayed;
CC      Name=b;
CC      IsoId=Q10651-2; Sequence=VSP_000017;
CC      Note=No experimental confirmation available;
CC      -!- SIMILARITY: Belongs to the APP family.
CC      -----
CC      This SWISS-PROT entry is copyright. It is produced through a collaboration
CC      between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC      the European Bioinformatics Institute. There are no restrictions on its
CC      use by non-profit institutions as long as its content is in no way
CC      modified and this statement is not removed. Usage by and for commercial
CC      entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC      or send an email to license@isb-sib.ch).
CC      -----
DR      EMBL; U00240; AAC46470.1; ALT_INIT.
DR      EMBL; U56966; AAA98722.1; -.
DR      EMBL; U56966; AAK68242.1; -.
DR      PIR; T15795; T15795.
DR      HSSP; P05067; 1MWP.
DR      WormPep; C42D8.8a; CE04209.
DR      WormPep; C42D8.8b; CE27845.
DR      InterPro; IPR008155; A4_APP.
DR      InterPro; IPR008154; A4_extra.
DR      Pfam; PF02177; A4_EXTRA; 1.
DR      PRINTS; PR00203; AMYLOIDA4.
DR      SMART; SM00006; A4_EXTRA; 1.
DR      PROSITE; PS00319; A4_EXTRA; 1.
KW      Signal; Transmembrane; Amyloid; Neurogenesis; Glycoprotein;
KW      Alternative splicing.
FT      SIGNAL      1      21      POTENTIAL.
FT      CHAIN       22     686     BETA-AMYLOID-LIKE PROTEIN.
FT      DOMAIN      22     621     EXTRACELLULAR (POTENTIAL).
FT      TRANSMEM    622     642     POTENTIAL.
FT      DOMAIN      643     686     CYTOPLASMIC (POTENTIAL).
FT      DOMAIN      205     228     ASP-RICH.
FT      DOMAIN      676     679     CLATHRIN-BINDING (POTENTIAL).
FT      CARBOHYD     84      84     N-LINKED (GLCNAC. . .) (POTENTIAL).
FT      CARBOHYD    201     201     N-LINKED (GLCNAC. . .) (POTENTIAL).
FT      CARBOHYD    249     249     N-LINKED (GLCNAC. . .) (POTENTIAL).
FT      CARBOHYD    417     417     N-LINKED (GLCNAC. . .) (POTENTIAL).
FT      VARSPLIC    538     539     Missing (in isoform b).
FT                                     /FTId=VSP_000017.
SQ      SEQUENCE    686 AA;  79434 MW;  A0816858FDD48608 CRC64;

      Query Match      22.3%;  Score 815.5;  DB 1;  Length 686;
      Best Local Similarity  29.1%;  Pred. No. 4.6e-33;
      Matches 222;  Conservative 109;  Mismatches 276;  Indels 155;  Gaps 22;

Qy      1  MLPGLALLLLAAWTARALEVPTDGNAGLLAEPQIAMFCGRLNMHMNVQNGKWDSDPSGTK 60
      :: || : :| | | | | | | | | | | | | | | | | | | | | | | | | |
Db      6  LMIGLLIPILVA-TVYAEGSPAGSKRHEKFIPMVAFSCGYRNQYM-TEEGSWKTDDERYA 63

Qy      61 TCIDTKEGILQYCQEVYPQLQITNVVEANQPVTIQNWCKRGRKQCKTHPHFVIPYRCLVG 120
      || | ||:||||: || : |||:| | : | |:| |:| | | | | | | | | | |
Db      64 TCFSGKLDILKYCRKAYPSMNITNIVEYSHEVSISDWCREEGSPCK-WTHSVRPYHCIDG 122

```

Qy 121 EFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTN-----LHDYGMLLPC 174
 || :|| || :| | | : || | : | | : : :|| ||
 Db 123 EFHSEALQVPHDCQFSHVNSRDQCNDYQHWKDEAGKQCKTKKSKGNKDMIVRSFAVLEPC 182

Qy 175 GIDKFRGVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVAEEEEV 234
 :| | ||||| || :| : | ::
 Db 183 ALDMFTGVEFVCCP----NDQTNKTDVQKTK----- 209

Qy 235 AEVEEEEEADDDDEDDGDEVEEEAEPEYEEATERTTTSIATTTTTTTESVEEVVRVPTTAA 294
 |::| ||||| | : ||::| ||
 Db 210 ---EEDDDDDDEDDAYEDDYSEESDEKDEE----- 236

Qy 295 STPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQVMREWEA-----ERQAKNLP 349
 | : | | : ||| |::| :| : ||::: :||:| | : |::||: |
 Db 237 -EPSSQDPYFKIANWTNEHDDFKKAEMRMDEKHRKKVDKVMKEWGDLETRYNEQKAKD-P 294

Qy 350 KADKKAVIQ---HFQEKVESLEQEAANERQQLVETHMARVEAMLNDRRLALENYITAL- 405
 | : | | ||: | ||:| |:: | ||:||||:::| | :| ||
 Db 295 KGAEKFKSQMNARFQKTVSSLEEEHKRMRKEIEAVHEERVQAMLNEKKRDATHDYRQALA 354

Qy 406 -QAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRSQVMTHLRVIYE 464
 | | | ||:|||| || : | : | ||: | : | || |
 Db 355 THVNKPNKHSVLQSLKAYIRAEKDRMHTLNRYRHLLKADSKEAAAYKPTVIHRLRYIDL 414

Qy 465 RMNQSLSLLYNVP-----AVA--EEIQDEVDELLQKEQNYSDDLANMISEPRISY 513
 |:| :||:| : | || : : ||| : | | | : | : |
 Db 415 RINGTLAMLRDFPDLEKYVRPIAVTYWKDYRDEVSPDISVE----DSELTPIIHDDEFSK 470

Qy 514 GN--DALMPSLT----ETKTTVELLPVNGEFLDDLQPWHSFGADSVPAANT---ENEVEP 564
 | | : | : :|| | : : : | | : : | : : |
 Db 471 NAKLDVKAPTTTAKPVKETDNAKVLPTASDSEEEADEYYEDEDDEQVKKTPDMKKKVKV 530

Qy 565 VDARP-----AADRGLTTRPGSGLTNIKTEE-----ISEVNLD 598
 || :| | | | | | : : || | | : : |
 Db 531 VDIKPKEIKVTIEEEKKAPKLVETSVQTDDEDDDEDSSSSTSSEDEDEDKNIKELRVDI 590

Qy 599 E-----FRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIATVIVITLVMLK 649
 | :|| | : | | : : : | | | :
 Db 591 EPIIDEPASFYRHD-----KLIQSPEVERSASSVFQPYVLASAMFITAICIIFAIT 642

Qy 650 KKQYTSIHGVEVDAAVTPEERHLSKMQQNGYENPTYKFFE 691
 : | :|| | ||||: || ||||| ||:
 Db 643 NARRRRAMRGFIEVD-VYTPEERHVAGMQVNGYENPTYSFDD 683

Search completed: July 26, 2004, 12:44:40
 Job time : 12 secs